THE Review of Gastroenterology

VOL. 20, NO. 12 DECEMBER, 1953

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NATIONAL GASTROENTEROLOGICAL ASSOCIATION

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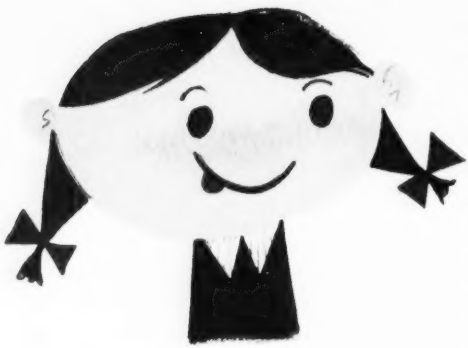

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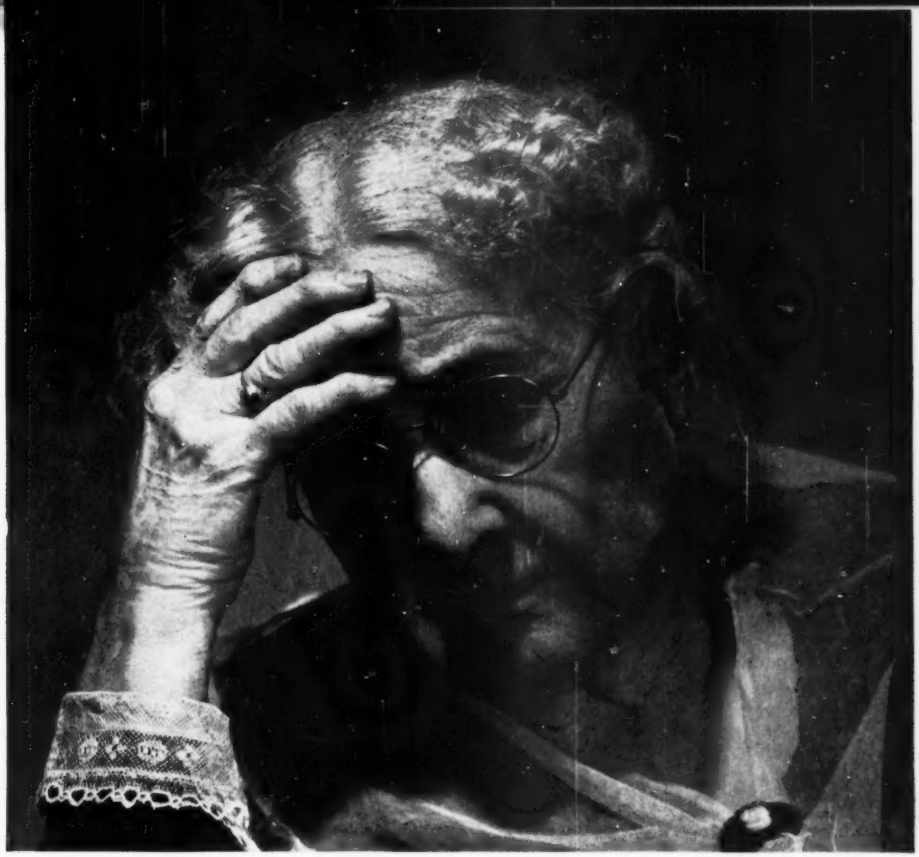

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The Review of Gastroenterology

(Incorporating the American Journal of Gastroenterology)

The Pioneer Journal of Gastroenterology, Proctology and Allied Subjects in the United States and Canada

contents:

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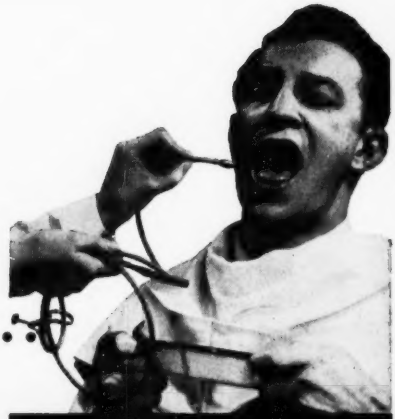

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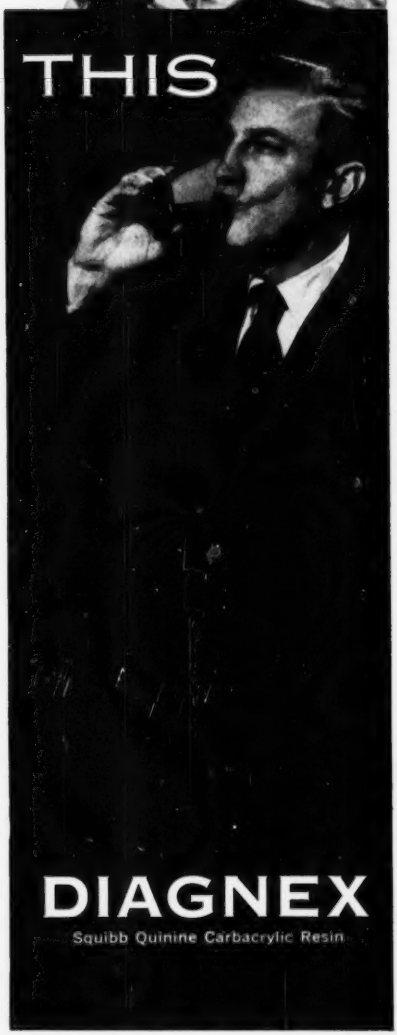

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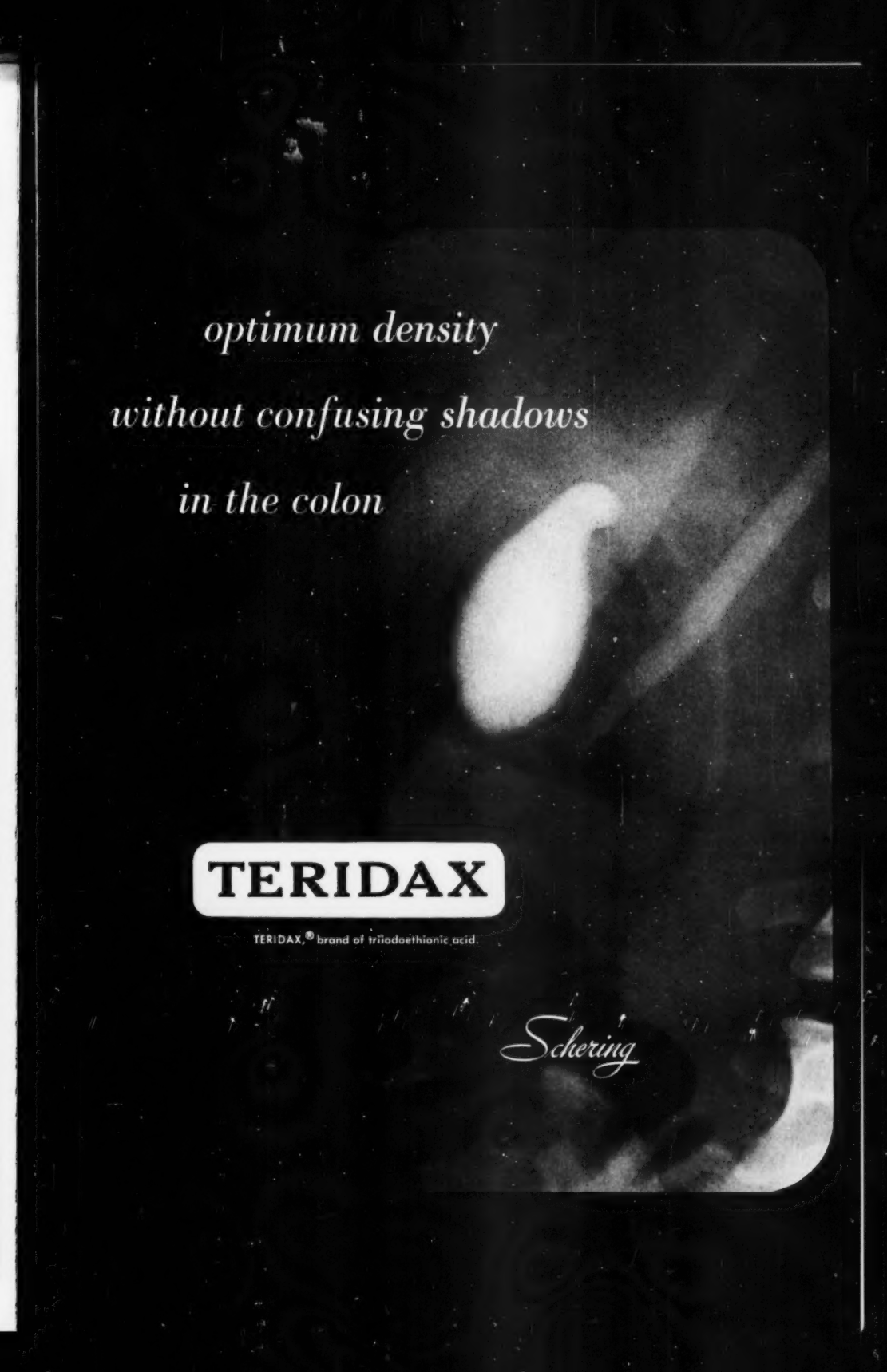
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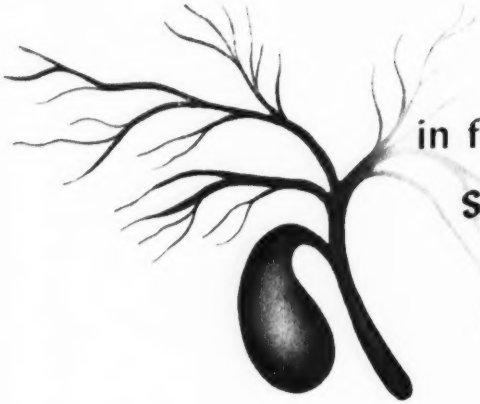

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DUODENOJEJUNAL DIVERTICULUM WITH DOUBLE GALLBLADDER OBSERVED IN TWO CASES

A. GALAMBOS, M.D.

New York, N. Y.

Diverticulosis of the small intestine is comparatively rare. It is much more frequent in the duodenum than in the jejunum or ileum. With the exception of the congenital diverticulum of Meckel the ileum represents the least frequent location. Diverticulum of the jejunum or of the duodenojejunal junction is a very rare finding. Its diagnosis is possible only by x-ray, which is rarely successful. In our opinion, the x-ray diagnosis, if it is carefully and properly made is not so rare. The condition is usually recognized only at the autopsy table.

We are reporting here two cases with a *large solitary diverticulum at the duodenojejunal junction coexisting with bifid gallbladder.* Both conditions are very rare and their combined occurrence in two patients constitutes a unique coincidence. Diagnosis was made *intra-vitam*, with the aid of x-ray.

CASE REPORTS

Case 1:—J. D., 67, female, married, white, first seen April 6, 1953 at our office. She has been suffering for 30 years with epigastric pain and discomfort, which "catches her chest from the back and irradiates toward the neck and head". Pain recurred through those years practically every day, especially in the evening hours. Since the last three or four months her complaints became continuous and nearly intolerable. The pain never was severe, cramp-like or agonizing. Her family and the attending physicians never gave any serious consideration to her suffering, because of its chronic character. Recently the persistent pain alarmed her family and she came to our office for "diagnosis". This patient never has been examined by x-ray. No vomiting, jaundice, melena or any ulcer syndrome-complex was ever present. She was suffering from headaches ever since she remembered. In recent years her condition became aggravated by frequent dizziness, limiting her daily activities. Clinical examination revealed a generally poor nutritional state and a secondary microcytic anemia with a 60 per cent hemo-

globin. Blood pressure read 180/110 which, during the time of observation, came down to near-normal level. Physical examination was otherwise largely negative.

The x-ray examination revealed a double gallbladder, which upon ingestion of fatty food promptly reduced its size, but did not disappear completely. Surprisingly the gallbladder, after 24 hours, was more sharply outlined than the first day. It was still sharper two days later, though it was no longer visualized on the 72 hour film. The double gallbladder on various films showed different configurations and at times unequal dye concentration was noted in the two chambers. The double gallbladder drained through one cystic duct.

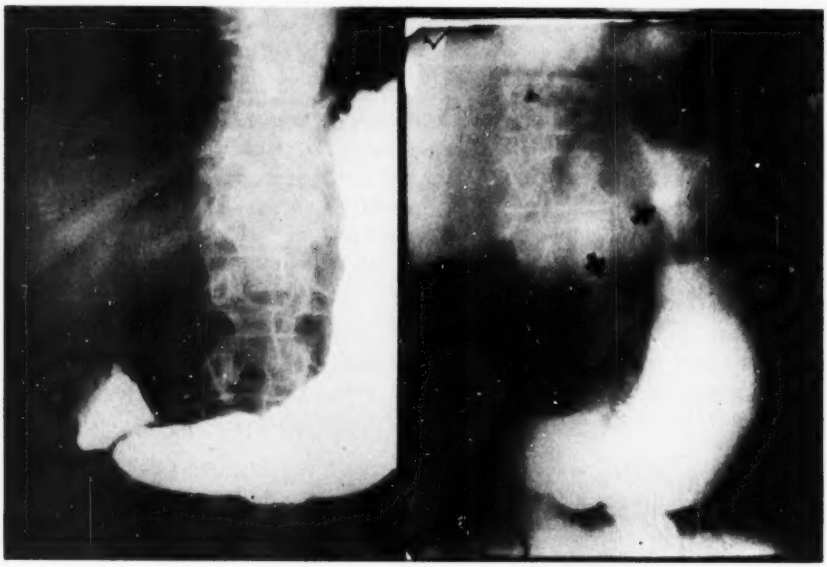

Fig. 1a Fig. 1b

Fig. 1a—Case 1. Immediately after barium filling of the stomach no diverticulum is seen.
Fig. 1b—Case 1. Few minutes later a huge diverticulum is visualized at the duodenojejunal junction. Strands of mucosal folds of this intestinal coil enter the diverticulum. Upper arrow shows a small gastric niche (ulcer or diverticulum).

The x-ray examination of the gastrointestinal tract revealed an ulcer niche-like bulge on the upper portion of the lesser curvature, visible only on the emptying organ. Its differentiation from a small gastric diverticulum was difficult. The fact that it did not disappear after a successful ulcer treatment, when diet and anticholinergic drugs promptly stopped the pain and the other complaints, would favor the diagnosis of diverticulum as against ulcer. In our experience an ulcer niche, upon effective treatment, nearly invariably promptly disappears.

Besides this small gastric diverticulum there was another huge round barium shadow noted in the concave area of the lesser curvature, topped by an air-bubble. This diverticulum, the size of a large egg, was not visualized immediately

upon the barium-filling of the stomach. The visualization of this huge sac became apparent only 60 to 90 seconds later, in the instant when the opaque material reached the duodenojejunal angle. This fact alone ruled out an ulcer niche or an accessory pocket on the lesser curvature. The mucosal folding of the gut at this junction could clearly be followed into the open-mouthed diverticulum. The stomach and the junction area fully emptied its barium content in an hour or so,

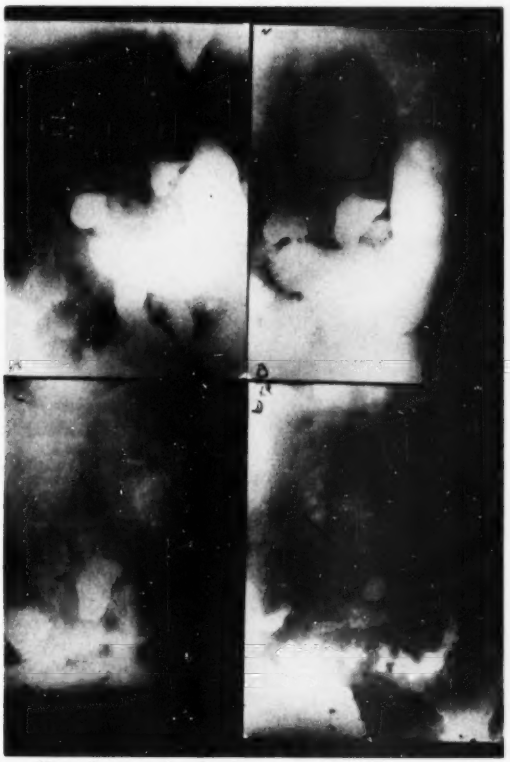

Fig. 2–Case 1. Four films showing the duodenojejunal diverticulum at various times after the barium filling.
A) Gas-bubble tops the diverticulum.
B) shows the gastric niche and the duodenojejunal diverticulum.
C) diverticulum fully visualized, after the stomach is emptied (90 min.).
D) diverticulum on a 5 hr. film.

but the isolated barium retention in the diverticulum was still demonstrable even on a five hour film. On the 24 hour film no barium retention, nor any gas accumulation was noted.

There was a marked redundancy of the sigmoid and of the transverse colon; the latter appearing in the relatively rare configuration of a double drooping.

Administration of Banthine Bromide (Searle) promptly stopped the pain and all the discomfort, which had intermittently annoyed this patient for so many years, and she remained free of any pain during the subsequent observation time of two months.

This patient was somewhat disturbed by the fact that no operation had been recommended for the gallbladder condition. As she stated that was the

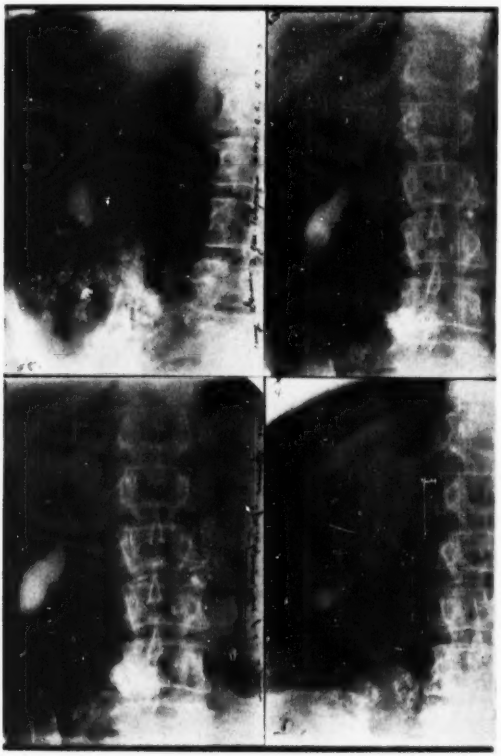

Fig. 3—Case 1. Double gallbladder. Four films showing various configurations.
A) Only one of the two chambers is clearly visualized; the dye concentration in the second chamber is very poor.
B & C) are postcenal films, shortly after the ingestion of the fatty meal.
D) 2½ hrs. after fatty meal. Great reduction in size.
Single cystic ducts visible on all films.

first case in her family's history that someone with gallbladder pathology escaped operation. We had to give her a good excuse.

Case 2:—F. T., female, married, 49, first seen on January 3, 1943. She was referred to us by her previous physician for "diagnosis". She was considered as one suffering from "rheumatism" and was under medical treatment for that

condition for the past 6 or 7 years by her previous attending physician and, at times, in one of the Medical Centers. She did not respond to diathermy, heat, lamp and injection treatments she received. We diagnosed this case as one of psychoneurosis. Physical examination was negative, except for a moderate osteoarthritis of the spine, which usually can be considered as inconsequential. No other signs of any rheumatic or rheumatoid arthritis were in evidence then, nor did she develop any since that time. Blood pressure, x-ray of the heart, EKG, oscillatory index, etc., were normal. The complaints referring to the arthritic condition soon receded and did not recur. However, she had constant complaints in kaleidoscopic variation. Hardly any organ or tissue in her body escaped her special attention, and often the most grotesque and fantastic complaints and symptoms developed and chased each other in incoordinated fashion. By the end of that year (1943) arterial hypertension started. Ever since, it gradually progressed. Readings as high as 240/130 were not uncommon in recent years. In 1951 she suffered two attacks of coronary occlusion, one in January and the other in July. Each time a posterior type of occlusion developed and resulted in myocardial infarction. EKG changes developed in typical fashion. In recent years endarteritis obliterans complicated the situation.

Complaints referring to the gastrointestinal tract were often in the foreground. Going back to 1943, during a routine work-up, a solitary diverticulum of the doudenojejunal junction and a double contoured gallbladder were found and diagnosed. These, however, did not seem to have caused too much annoyance. Sometimes for years no complaints referring to the gastrointestinal tract were even mentioned. A few months ago upper abdominal complaints recurred and at the reexamination the duodenojejunal diverticulum and the double gallbladder were restated as they were found 10 years ago. It was considered that most of her complaints were not related to these, most probably, congenital anomalies. She responded to medical treatment each time.

Historical Data

Reference is made to author's work on "Diverticulosis and Diverticulitis of the Colon" in The Review of Gastroenterology.

Frequency:—Case made barium meal studies in 6,847 cases and while the duodenum harbored diverticulum 85 times, this was found in the jejunum only four times and once each in the jejunum and ileum. Edwards found diverticula in the jejunum after barium meal ingestion, only four times among 4,631 cases, an incidence of 0.086 per cent. Rankin and Martin report the findings of the Mayo Clinic after 72,715 roentgen ray examinations of the gastrointestinal tract. Diverticulum was found in the duodenum 111 times, but only three times in the jejunum, a ratio of 1 to 24,238. As against this, the ratio in the colon was 1 to 17, with an occurrence of 1,562 among 27,006 barium enema cases. In necropsy material Browne and McHardy encountered jejunal diverticula 16 times among 8,000 cases, an 0.2 per cent incidence. Edwards noted jejunal diverticula among

2,820 autopsy cases 9 times (0.31 per cent). Later this rate was increased to 0.51 per cent among 881 cases of new postmortem studies, when special attention was focussed on searching for small intestinal diverticula. Jenkinson found jejunal diverticula only three times among many thousands of cases examined by x-ray. Feldman states an autopsy incidence of jejunal diverticula at 0.02 per cent, while the roentgen incidence is estimated to be about 0.05 per cent. This seems to be a *situs inversus*, inasmuch as it would indicate that the pathologist can corroborate the existence of these diverticula only in 40 per cent, i.e. 4 times out of 10 cases diagnosed by x-ray. Actually, just the opposite must hold

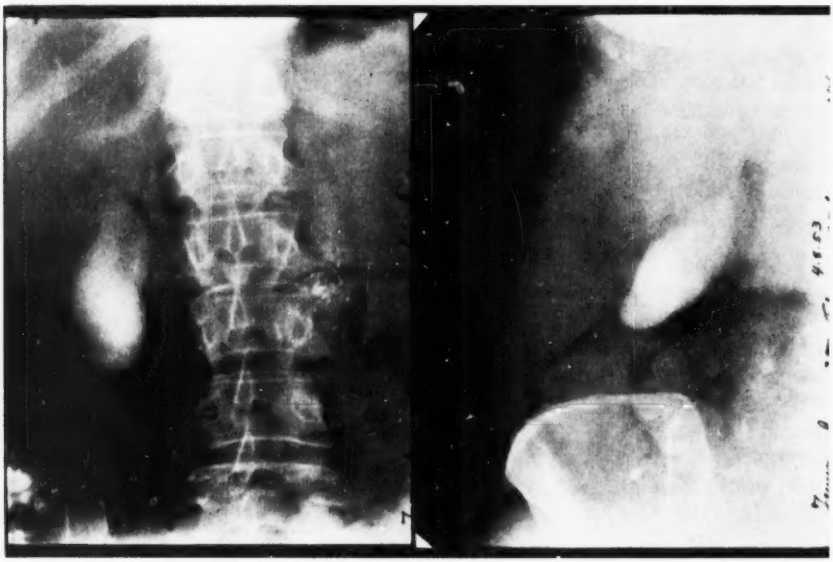

Fig. 4a Fig. 4b

Fig. 4a—Case 1. 5 minutes postcenal.

Fig. 4b—Case 1. 24 hours postcenal.

The double contours are sharply visualized. They vary in shape.
The size of the gallbladder is greatly enlarged, after the sharp contraction on previous day (reabsorption).

true as the x-ray diagnosis succeeds only in a relatively small percentage of the cases proven by autopsy, the majority remaining undiagnosed.

The double gallbladder is a great rarity in the human. Graham et al did not observe a single case among 1,218 cholecystographic examinations. Boyden found it only 5 times in 19,000 cases. It is conceded that the prevailing type of the double gallbladder in the human is that of a truly double gallbladder with two individual cystic ducts. The bifid or bilobed gallbladder, the second variety in which the not fully separated chambers drain through one cystic duct is,

according to the observations of Boyden and also of Gross and others, a still greater rarity. Both of our cases seemed to belong to this latter group.

Pathology:—According to the generally accepted theory diverticula in the jejunum develop, as they do in other locations of the gastrointestinal tract, at the site of their predilection, i.e. the site of least resistance. A precondition is an increased intraluminal pressure. According to Fraser this is specifically true for the diverticulosis of the jejunum. The site of least resistance is identified as the one of muscular deficiency, or a hiatus, which may represent a congenital weakness, or it may be conditioned by the entrance of the mesenteric vessels in the gut (Klebs, Edwards, etc.). First, the entire wall, covered by all the coats of

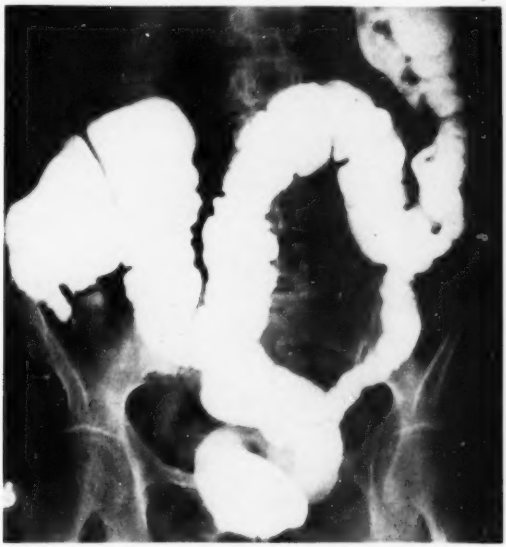

Fig. 5—Case 1. Barium enema. Redundancy of the colon, in the splenic flexure and sigmoid is moderate; the redundancy of the transverse colon is huge, presenting itself in double drooping.

the bowel is taking part in the pouch formation. Only later, with the gradual increase in size, the muscular layer suffers a pressure atrophy and slides off the side and finally at the base of the pouch the muscular sheeting is missed and the wall consists of the mucosa and serosa only. Edwards considers the absence or deficiency of the muscular coat as the criterion for the pouch being of acquired nature. According to him the pouches are closely related to the mesentery and the diverticula nearly always push their way between the leaves of the mesentery. In Edwards' description the formation of sacculation starts with a pair of pouches, one on either side of the line of mesentery and, as the pouches grow, they meet in the mesentery and the strip of tissues separating them will be taken up and the two pouches fuse. Finally, due to the continued

intraluminal pressure a single, smooth-walled large diverticulum results. Rankin and Martin do not agree with this developmental theory. They found the diverticula usually at the opposite to the mesenteric border, or laterally to it.

Congenital gallbladder pathology covers a large field. Bockus estimates that in about 10 per cent of the cases one or several congenital pathology of the gallbladder may be present, amenable to present day x-ray diagnosis. Duplication of the gallbladder with one or two cystic ducts in the well defined cases offers no diagnostic difficulties. The same holds true for the diverticulum of the gallbladder. "Phrygian cap" which represents the most common congenital

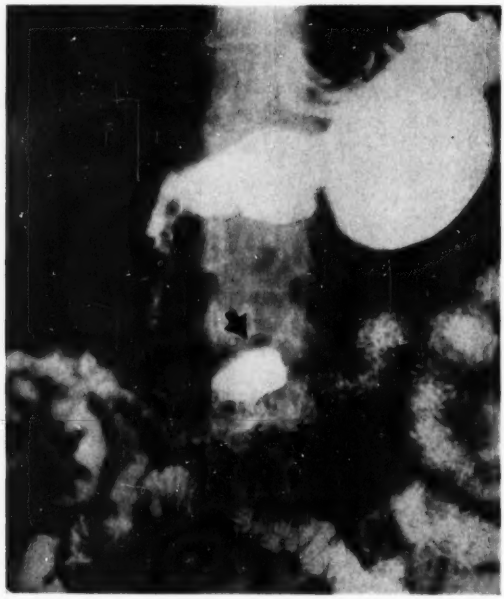

Fig. 6—Case 2. Prone position. The duodenum, resp. its third portion goes straight, without angulation into the jejunum.
There is a huge, solitary diverticulum at or near the duodenojejunal junction. Strands of mucosal folds enter the diverticulum.

anomaly is not difficult to recognize. In all of these conditions, however, in the presence of common fascial and peritoneal coat, diagnostic difficulties may be encountered. The true nature of the underlying pathology may be disguised, and the surgeon would find it difficult to properly recognize this anomaly. It may be missed even at a p.m. examination. Only the x-ray is diagnostic.

A deep bend caused by a distinctive fold in a mild case may produce the appearance of a "phrygian cap", usually located across the long axis, on the median side of the gallbladder. If the deep bend cuts the organ into two chambers

along its longitudinal axis, a bilobed gallbladder is the result. If a diverticular outpouching, which may be larger than the gallbladder itself, is the pathological occurrence, bisegmentation or biloculation will likewise be noted and their differentiation from each other in rare cases may be difficult or arbitrary not only to the roentgenologists but eventually even at the autopsy table.

While the "phrygian cap" is relatively not uncommon, the diverticulum is rare, double gallbladder is still rarer, and the latter's subgroup, that of the bilobed gallbladder seems to be the rarest of all.

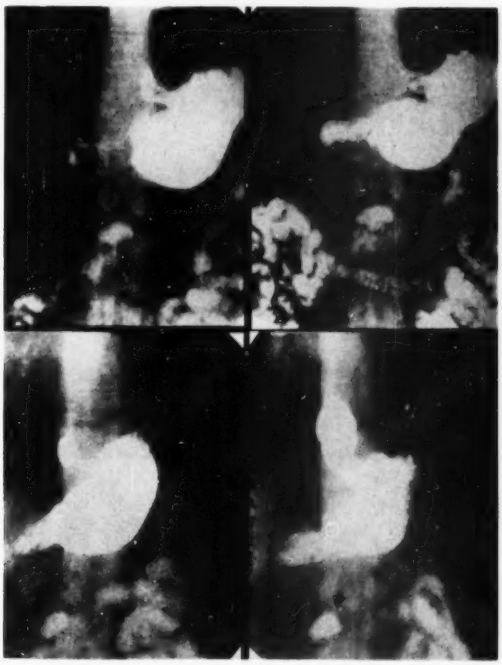

Fig. 7—Case 2. Four films taken in prone position, all showing the fully visualized solitary diverticulum of the duodenojejunal junction.

Prone position in this case proved to be superior to the erect posture for the visualization of the diverticulum.

Number and size of the diverticula:—Jejunal diverticula are single or multiple. The ratio between the two found by various authors is quite contradictory. The multiple type seems to preponderate roughly at a ratio of 2 to 1. Sir Astley Cooper who first described this lesion in 1844, found numerous pouches in his case. The case of Osler (1881) harbored 55 diverticula in the upper jejunum, varying in size from a cherry to a large apple. Hansemann's case referred to a man of 85 who contained about 400 diverticula in the small intestine. Edwards

found a variety between pea and chestnut sizes. It is generally conceded that both the solitary and the multiple variety is most frequently found in the upper portion of the jejunum. Diverticulum in the ileum is very rare. The duodenum, especially its second portion, harbors these pouches fairly often, second only to the colonic localization; it is rare in its third segment and the fourth portion contained it only in 0.5 per cent of 500 duodenal diverticula (Feldman). According to this tabulation diverticulum in the fourth portion is even rarer than its occurrence in the jejunum. The duodenojejunal angle is an exceptional location for diverticula. Feldman in his book reports it once, and in Buckstein's case there were two diverticula near this junction. A single large diverticulum in both of the cases presented here was located at this junction. Since Case first described diverticulum at this junction, every author stresses the diagnostic difficulty of its x-ray demonstration and, if it is successful, its differentiation from the

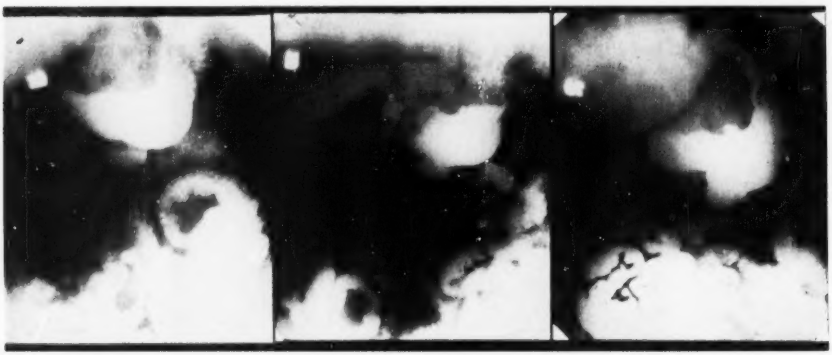

Fig. 8a Fig. 8b Fig. 8c

Fig. 8—Case 2. Diverticulum of the duodenojejunal junction, visualized in erect position. The diverticula are not as clearly demonstrated as they were in the prone position.
a) diverticulum, with gas bubble, seen on the emptying stomach.
b) demonstration of the diverticulum is still less clear.
c) diverticular shadow confluent with the gastric opacity.

Haudeck's niche, or an accessory pocket of an ulcer of the smaller curvature. It was relatively easy to rule out these contingencies in both of my cases.

Age:—Diverticulosis usually affects the older age group. The mean average age is between 55 and 60 years. The mean average is calculated as the age of discovery of the case. Onset is practically impossible to state.

Diagnosis is possible only through the x-ray demonstration of the diverticula. "Unlike duodenal diverticula, pouches lower down than in the small intestines are difficult to detect by roentgenography, except in the comparatively rare cases, in which there is retention of barium in them, and they will, therefore, be more often missed than not" (Edwards). That represents the general consensus. Demonstrability largely depends upon the relation of the pouch to the gut. If the mouth is wide and there is a large opening from the gut into the diverticulum,

as is usually the case, the barium cannot be retained in the pouch, and its x-ray demonstration will suffer. In these cases no clinical symptoms are expected to develop. If, however, the mouth is relatively narrow, then the opposite holds true. In these cases clinical symptoms do develop, as a rule, because in the larger pouches stagnation, fermentation, and inflammation may set in, and the diverticulosis transforms into diverticulitis, a proper designation originating from Case. The x-ray demonstration of the larger diverticula with narrow neck permits beautiful pictures, the opaque diverticulum sitting on the gut, like a mushroom, or a queen's crown (former being more often seen now-a-days than

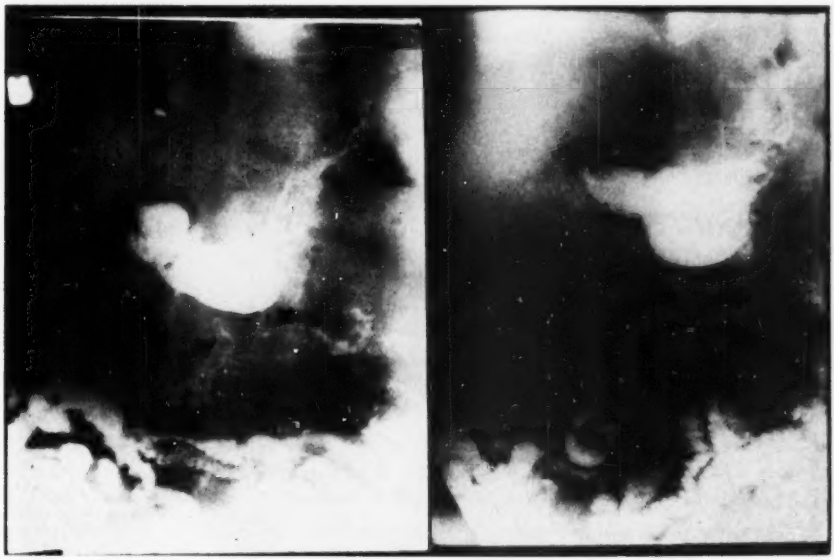

Fig. 9—Case 2. The diverticulum, on both films, just emptied its barium content. At its site slight barium remnants, in saucer shape, denote the outline or the silhouette of the diverticulum. Without knowing the facts as they pertain to the diverticulum and its location, no diagnosis could be made.

the latter). The mucosal folding, strands of folds, can often be followed from the gut into the pouch. The latter is often topped by a gas bubble, or even three strata may occasionally be seen. The erect position warrants better preconditions for a successful visualization (Case). There are, however, exceptions, as e.g. the second case presented here. The multiple fluid level must sometimes be differentiated from similar findings due to multiple small obstructions in case of tuberculotic peritonitis (Koehler), or even from fluid levels in small intestinal obstruction.

The diagnosis of the bilobed gallbladder is, likewise, an x-ray diagnosis. Its differentiation from a double gallbladder, from a diverticulum of the gall-

bladder and from a phrygian cap may be difficult. The two chambers may be distinctly and separately visualized, or they may superimpose upon each other. The one chamber may take up more dye, or concentrate better, giving clearer and sharper images than its mate. The one can contain stones or show other pathology, with a relative immunity of the other chamber. Sometimes the changes in configuration are more pronounced and the relation of the chambers to each other may clearly manifest itself after the size of the gallbladder is reduced upon administration of fatty food.

Clinical Picture

There are no pathognomonic clinical symptoms, no distinguishing features in jejunal diverticulosis. Symptomatology depends primarily on the anatomical relation of the pouch or pouches to the jejunum. In a case with narrow opening, the barium, upon entering the diverticulum, may be retained for many hours after the complete evacuation of the gut. This isolated visualization is very characteristic. With such anatomical constellation retention, inspissation, fermentation, inflammation and finally even hemorrhage and perforation, etc., may develop, as it would in a diseased appendix or colonic diverticulum. Under such conditions pain, symptoms of indigestion, vomiting, fever, chills, malaise, etc., may be observed. Undefined, obscure epigastric pain, resisting routine treatment is the most common symptom, which may be present even in uncomplicated cases, especially if the retention in the pouch is marked and the disease is extensive.

The clinical picture of the bifid gallbladder depends upon the anatomical and functional conditions of that organ. If only the congenital anomaly is present with a normally functioning gallbladder, a bifid gallbladder would produce no clinical symptoms. This was the observation in both of our cases. The fact, that 24-48, even 72 hours after the ingestion of telepaque the visualization of the gallbladder still persisted, in spite of the fact that it promptly reduced its size after the first fatty food given, should increase our interest in such behavior. The present day conception explains this phenomenon by the reabsorption theory. It is not considered "per se" as pathology of any consequence.

Discussion

Ian Fraser quotes the Century and Oxford Dictionary, in consulting it for the definition of the term "diverticulum". It is defined as a "way-side shelter or lodging", with the underlying meaning that they are houses of ill repute where trouble is apt to brew. And trouble does brew in the gastrointestinal tract diverticulum, but not necessarily so. In jejunal diverticulosis clinical importance is only attached to those cases in which the foramen is narrow and the sac is large. In such cases the large and filled sac hangs down on either side of the gut, the neck becomes kinked and the entrance is cut off. With the occlusion of the neck there is a subsequent stasis, putrefaction, gas formation, clinically

manifested by borborygma, distention and flatulence (Fraser). When the opening is wide, no retention develops and the diverticula are, as a rule, not visualized by x-ray. In such undiagnosed cases clinical symptoms are less prone to develop.

The jejunal diverticula are, according to the experimental work done by Fraser, etiologically different from the sacculations of other localizations in the gastrointestinal tract. He subjected the fresh postmortem gut to distention under uniform pressure. The results in all his experiments were likewise, identical and consisted of formation of diverticula at the upper segment of the jejunum, only. All the other portions of the gastrointestinal tract remained free from sacculation. The experimentally produced diverticula of the jejunum fully resembled those

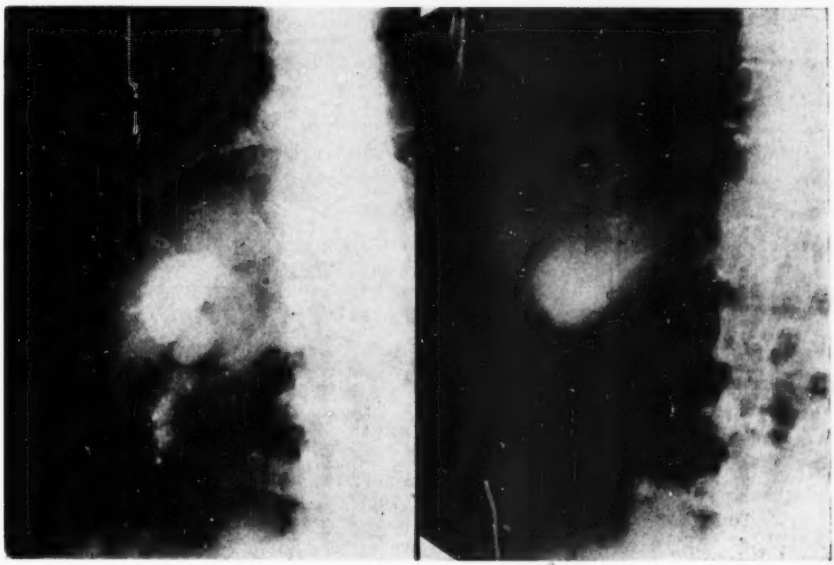

Fig. 10a Fig. 10b

Fig. 10—Case 2. Double gallbladder. Various configurations on both films.
a) 40 min. postcenal.
b) 72 hours postcenal.

found in their clinical counterpart. The herniation of the mucosa through the muscle always developed along the mesenteric border and between the leaves of the mesentery. This experience supported the mesenteric theory of Klebs and Edwards, at least as far as the jejunum was concerned in the formation of the diverticula. In Fraser's opinion the jejunum is the only location in the gastrointestinal tract in which diverticula do develop as a result of an increased intraluminal pressure, due to distention.

In the first case presented here the patient had suffered for thirty years from obscure pain, discomfort and gaseous distention in the epigastric region. No-

diagnosis had been established during those years. A routine gastrointestinal x-ray series revealed a huge, large egg-sized, solitary diverticulum in the lesser curvature region, which had to be differentiated from an accessory pocket of a gastric ulcer. This diverticulum was not visible right after the barium filling of the stomach. It took about one and a half minutes before the barium, upon entering the duodenum, reached the duodenojejunal angle and, at this moment, it promptly filled the sac. The mucosal folding of the junction region could easily

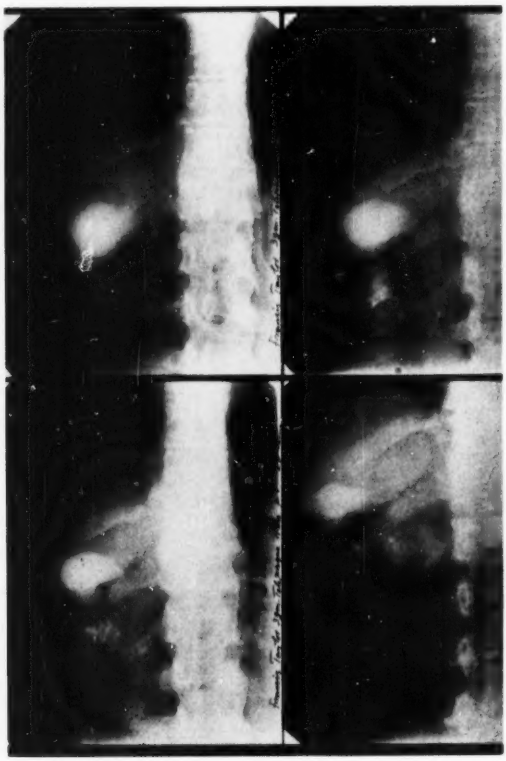

Fig. 11–Case 2. Double gallbladder. Various configurations on all four films. Similar pictures were obtained 10 years ago.
Differentiation from huge gallbladder diverticulum may represent a diagnostic challenge, although the films shown in Fig. 5 rule out this diagnosis.

be followed into the diverticular cavity. Even though the barium left the stomach and the junction in about an hour, the diverticulum could be clearly seen even after five hours. The erect position proved to be superior for the technic of visualization of the sac, as well as also of the gas bubble on the top of the sac. Pain and all the discomfort promptly stopped upon administration of Banthine Bromide and did not return up to the subsequent observation two months later.

The second case was that of a highly nervous type of a woman. She often manifested the most unusual complaints, ostensibly unrelated and unproportional to the underlying pathology. She uttered fewer complaints during a painful seizure caused by acute coronary occlusion, than at any other time. She never was without complaints. She responded to medical treatment each time and, consequently, the beneficial effects of the anticholinergic drugs and that of the diet could only be evaluated with certain reservation.

In this case the duodenum, as a result of some congenital anomaly failed to form an angle upon joining the jejunum; it flatly continued into it. Both the duodenum and the jejunum, as well as their junction, remained below the greater curvature throughout. In erect position the duodenojejunal diverticulum could not be seen, because the sac extended upward and it was overshadowed by the barium in the stomach proper. Only 30 to 60 minutes later when the greater part of the barium had already left the stomach, which in its entirety had moved higher up, could the doudenojejunal diverticulum be demonstrated. It usually contained a gas bubble. In this case the prone position proved to be superior and more reliable for the diverticular visualization than the erect position. In the prone position with the stomach half emptied, the diverticulum was easily and fully visualized, and the strands of rugae were in evidence.

The medication and diet indicated for the jejunal process seemed also justified for the gallbladder condition. There was no serious functional disturbance present and no surgical consideration came up for either.

Graham-Cole's method is indispensable for the x-ray demonstration of the gallbladder, and the recently introduced telepaque (Winthrop-Stearns) enables a far superior visualization than any other drug used in the past. Often the cystic, common and liver ducts are also well visualized a few minutes after the gallbladder contraction started upon the administration of fatty food. Three, and even 5 or 6 grams are usually well tolerated.

While we considered the diagnosis of a bifid gallbladder as most probable in both cases, nevertheless, on grounds of roentgenological evidence, a huge diverticulum of the gallbladder could *a limine* not be ruled out in either of the cases. Which of the two was the actual pathological substrate, could not be stated with any degree of accuracy, but the difference was a rather academic one.

Summary

Two cases of solitary, huge duodenojejunal diverticulum in combination with bilobed gallbladder are reported.

The rarity of the solitary diverticulum at the duodenojejunal angle as well as that of a bifid gallbladder, especially their combined occurrence in two cases, has been stressed.

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COMMON SENSE MANAGEMENT OF ENTEROBIASIS

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Pinworm infestation is almost as widespread as the common cold, and presents a challenge to the general practitioner, the pediatrician, and the proctologist. Many procedures have been proposed for the treatment of enterobiasis, but it is recognized that the correct choice of medication is merely the first step toward eradication of the disease. Permanent control of this vexing affliction calls for the prevention of reinfestation by means of hygienic and other measures. Only an integrated plan of management holds out the promise of a cure, and will spare the patient the disappointing experience of repeated unsuccessful treatments. It may, therefore, be of practical interest to review briefly the subject of enterobiasis, and to examine the various therapeutic measures available.

The Life Cycle of Enterobius Vermicularis

An effective program to rid the patient of *Enterobius vermicularis* depends on an adequate understanding of the life cycle of the parasite, inside and outside of the human host. The common pinworm or seatworm matures exclusively in the human intestines, and all attempts to reproduce its life cycle in animals have failed. Infestive pinworm eggs enter the mouth of the host by ingestion or inhalation. Once they have reached the bowel they develop into full-sized worms which soon mate. While the male of the species dies off, the gravid female migrates to the anal opening and ejects approximately 11,000 eggs. The life cycle of the pinworm within the human host, from ingestion of infestive eggs through maturation to deposition of new, not yet infestive eggs, is between 15 and 28 days[5].

Studies on enterobiasis among boys at a summer camp disclosed that gravid pinworms may be found about one inch above the mucocutaneous junction at 8 p.m.; by bedtime (9 p.m.) they had reached the junction; one-half hour later they could be found on the moist perianal skin, up to a distance of two and one-half inches from the anus, and as far forward as the scrotum. Exposure of the female pinworm to the outside air results in forceful expulsion of eggs which scatter over a wide region. Some females die following oviposition, and shriveled bodies can sometimes be recovered in the morning[2].

Fertile eggs measure 50 to 60 by 20 to 30 microns[4]; they are elongated, asymmetrical, flattened on one side, with thick, slightly opalescent shells, and contain a coiled larva. These larvae are not yet infestive, but become so within six hours at body temperature, while the same development may take up to 30 hours at normal room temperature (68° F.)[5]. Pinworm eggs retain their ability to enter into the infestive stage longer in a humid environment than in

dry air, and thrive in cool and moist weather. A temperature of 149° F., with a humidity of 20 per cent will prove lethal within one minute, while the eggs will withstand freezing for several days. Such considerations of the survival of potentially infestive eggs, however, are largely of theoretical importance. In most cases pruritus produced by the irritating fluid surrounding the enterobius eggs causes the patient to scratch, thereby transferring them to the fingers, whence they reach the mouth, starting a new cycle of infestation.

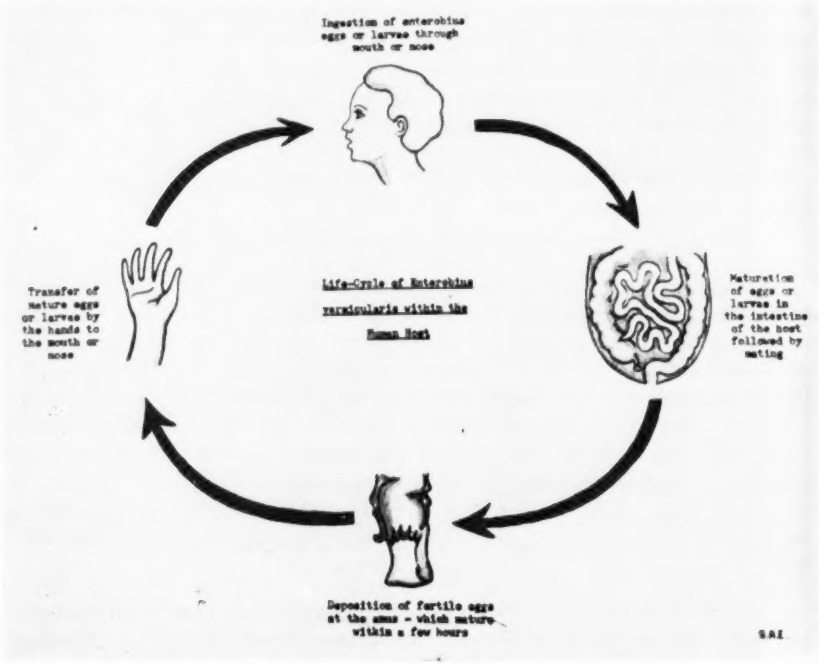

Fig. 1

The Incidence of Enterobiasis

In the United States, between one-third and one-half of all children of school age harbor pinworms. The incidence is lower in pre-school years, and recovery is apparently spontaneous in adolescence. Reinfestation of adults, however, is common following introduction of pinworms into the home by the children. Enterobiasis is found at all levels of the population, and in persons of all races. It is less frequent in Negroes than among Caucasians[6]. The rate increases in congested areas, and still more in families of large size, but decreases with improved sanitation of the home[8].

Signs and Symptoms

Well over half of the children with enterobiasis present no complaints whatsoever, and pinworms are accidentally found in the perianal region or detected in the course of routine laboratory examinations. The most characteristic symptom of pinworm infestation is pruritus ani after the child has retired for the night. Vaginitis is apt to develop when gravid seatworms enter into the genital tract. Perianal and vaginal irritation is often accompanied by secondary infection due to scratching. Other symptoms include insomnia, restlessness during sleep, nocturia, burning upon urination, vague abdominal pain, vomiting, diarrhea, and anorexia. Children with enterobiasis often have dark circles under their eyes, are pale, listless, and underweight. They may show various behavior problems, especially guilt feelings, lack of cooperation and concentration, which occasionally are wrongly interpreted even by trained observers[24]. Ordinarily such secondary effects are corrected by eradication of the parasites; the children gain weight, improve in social adjustment, and obtain better grades at school[5].

Nervous manifestations, like nose-picking, teeth-grating, tics, thumb-sucking, and nail-biting are no more common in infested than in non-infested individuals. Thumb-suckers and nail-biters, however, are more likely to ingest pinworm eggs lodged under the finger nails or present on contaminated fingers, and are, therefore, usually susceptible to enterobiasis.

A clinical finding suggestive of enterobiasis is slight vaginal discharge in the morning. Scratch and intradermal tests, and various types of blood determinations, on the other hand, have proved of little value. The diagnosis is therefore based on the demonstration of enterobius eggs and—more rarely—on the finding of living or dead pinworms.

Diagnosis

By examination of the feces it is possible to detect only those rare cases in which eggs have been deposited in the bowel, and the procedure has therefore been abandoned[13].

Much more reliable results are obtained by the perianal technic, founded on the observation that although pinworm eggs are usually scattered over a wide area, the egg yield is most profuse at the junction between the moist mucosa of the anal canal and the somewhat dry, waxy perianal folds. Three different procedures are in use for the collection of specimens for microscopic examination: (1) scraping with a cellophane swab; (2) blotting with scotch tape, and (3) direct application of a glass slide. Whichever technic may be chosen, material must be collected first thing in the morning, immediately after awakening, and before the patient goes to the bathroom. In the presence of negative findings the test should be repeated; material may have been removed during the silent period in the life cycle of *Enterobius vermicularis*, in which no eggs are present

at the anal opening, and testing must be continued intermittently for a maximum of 28 days.

For scraping, the NIH (National Institute of Health) *swab* is used. It consists essentially of a piece of cellophane wrapped around the tip of a glass rod[11]. Starting at the anal ring, the swab is carried outward with firm strokes, parallel to and within the perianal folds. In order to protect the specimen the swab is then inserted into a test tube. At the laboratory the cellophane is removed from the glass tip and mounted on a slide for microscopic examination.

For blotting, a strip of *scotch tape*, adhesive side out, is firmly attached to the tip of a tongue depressor[14]. The patient is asked to spread his buttocks, and the tip of the spatula is gently pressed against the anal and perianal regions. After the patient has released the buttocks for one minute, the applicator is withdrawn. The scotch tape is then mounted on a slide and studied under a low-power microscope. If the specimen contains only a small number of eggs, a single drop of toluene, inserted between the sticky tape surface and the slide, will clean away everything but the pinworm eggs and facilitate identification.

If a *glass slide* is applied directly to the anal and perianal areas, the moisture of the anal mucosa will cause some eggs to adhere to the slide. The specimen is dried before examining it under the microscope.

For obvious practical reasons many physicians prefer to have the parents take the samples themselves in the morning when the child awakens. If, however, the sampling is to take place at the doctor's office, the parents should be instructed not to bathe the child before examination.

Evaluation of Anthelmintics in Common Use

Pinworm eggs become infestive so soon after they have been deposited, that medical treatment is directed toward destruction of the parasites before oviposition has occurred. The remedy used to this end must be reliably effective without at the same time producing toxic reactions. A great variety of drugs have been proposed and will be discussed briefly in the following.

Carbon tetrachloride and *tetrachlorethylene*, which are in use for other types of intestinal helminthiasis, are generally of no value in the presence of pinworms[8]. It must be added that tetrachlorethylene has proved reasonably effective in the control of slight cases of enterobiasis[5]. But the side reactions observed—drowsiness, abdominal cramps, diarrhea, anorexia, and asthenia—far outweigh the therapeutic benefit of the drug.

Santonin has occasionally been tried for the eradication of *Enterobius vermicularis*. Its effectiveness, however, is so limited that there is no good reason for exposing the patient to the grave toxic reactions attending administration of santonin[9].

Hexylresorcinol (Caprokol), the medication of choice in ascariasis, has been used in the treatment of enterobiasis in various forms: as pills or capsules taken by mouth, as a rectal enema, and as a jelly, introduced into the anus at bedtime. Some observers found enemas more effective than hexylresorcinol administered orally[14], but others have discontinued use of this drug in all its forms[8].

Early tests with *phenothiazine*[15,16] proved very successful, but the drug is potentially dangerous, and toxic manifestations include skin reactions, fever, hepatitis, renal damage, tachycardia, and anemia, which in one reported case ended fatally[19].

Quinacrine hydrochloride (Atabrine) has been recommended as a one-day treatment for enterobiasis[21]. No food is permitted the night before treatment, and the entire dose of 10 mg. per kilogram of body weight should be given orally in the morning on an empty stomach. Three hours later a purgative is administered. Atabrine, however, can be recommended only with strong reservations, since according to some investigators acridine compounds are likely to produce severe toxic symptoms which far outweigh the usefulness of these preparations.

Tripelennamine hydrochloride (Pyribenzamine) is fairly effective in the eradication of pinworm infestation, and cures have been reported at a rate of between 56 and 80 per cent[14]. Pyribenzamine is given as an elixir in a daily dose of 2 mg. per pound of body weight, in three equal portions before meals. Untoward side-effects include drowsiness, excitement, anorexia, and leukopenia. A further disadvantage is the repulsive taste of the drug.

Diphenhydramine hydrochloride (Benadryl), another antihistaminic agent, and originally used for the control of asthma, also possesses anthelmintic properties[23]. In a small series of cases Benadryl, administered in the form of tablets with enteric coating, proved quite effective in the control of oxyuriasis, but the drug has the same side-effects as Pyribenzamine, and will occasionally produce palpitation and gastric irritation[3].

Parabenzylphenylcarbamate (Diphenan), in combination with hexylresorcinol enemas, has been successful in 77 per cent of cases[14]. The drug is administered after the three daily meals, in pleasant-tasting wafers, the dose varying with the age of the child. The course of treatment consists of two 14-day periods, with one week's rest in between. Diphenan should not be prescribed in the presence of kidney disease, but otherwise produces no untoward side-effects. Its cost, however, is prohibitive.

Gentian violet, an aniline dye, was formerly considered superior to any other medication for enterobiasis[7], but more recent reports are far less enthusiastic, and some have arrived at a cure-rate of less than 18 per cent[8]. The drug is preferably prescribed in the form of tablets with a four-hour enteric coating, the dose depending on age and weight of the patient. Three tablets a day are administered, and medication is continued for three weeks, interrupted by a rest

period of one week; according to another plan it extends over two 14-day periods, with one week's rest in between. Although gentian violet is less toxic than many of the other preparations used for pinworm infestation, anorexia, nausea, epigastric pain, diarrhea and vomiting may follow its administration[21]. In one series approximately 39 per cent of patients suffered from gastrointestinal upsets[5]. On account of this toxicity, and because the dye is not effective in all cases, medication with gentian violet is no longer the treatment of choice, though it still retains some value as an alternative procedure.

Infusion of *quassia chips*, administered as an enema, relieves symptoms of pinworm infestation, but cannot be relied upon to exterminate the parasite[5].

It would serve no useful purpose to discuss each and every one of the drugs more recently tried for the treatment of enterobiasis. In passing it might be mentioned that tests with sulfonamides proved discouraging, while Butolan and Lubisan gave promising results[22].

Terramycin hydrochloride was administered to patients suffering from pinworm infestation; but this medication, though successful, had to be discontinued on account of undesirable side-reactions. When the intermediate amphoteric form of terramycin, *terramycin base*, was substituted, it proved very effective in 52 cases[18]. The drug is administered in single daily doses, graded according to the age of the patient, for a period of seven days. Terramycin base results within 48 hours in morphologic changes of the pinworm eggs, an increasing number of which are immature and incapable of development to the infestive stage. After a few days no further eggs can be detected. Terramycin base does not seem to be toxic, but as experience with this antibiotic is as yet limited, clinicians will do well to test the patient for hypersensitivity to the drug before starting treatment.

Reviewing the foregoing long list of drugs used for pinworm infestation, there seems to be no valid reason to recommend treatments which are either unreliable, expensive, or irritating, and often even potentially dangerous. Patients who have experienced the toxic side-effects of certain anthelmintics frequently prefer to keep the worms rather than take the cure. It is, therefore, not surprising that physicians have again turned to the oldest pinworm remedy of all: garlic.

Garlic is administered raw, in the form of deodorized tablets, or as a rectal suppository. Raw garlic can be given in any form acceptable to the patient. One clove, grated, and mixed with grated carrots and mayonnaise is placed in a sandwich. Children like the remedy in this pleasant form. Raw garlic is taken every other night with the evening meal or at bedtime for two 14-day periods, interrupted by one week's rest[14]. The primary objection to the use of raw garlic is, of course, its lingering odor, but fresh parsley eaten immediately afterwards will serve as a natural deodorant.

Rectal suppositories combining oil of garlic with oil of eucalyptus and cocoa butter may take the place of oral administration of raw garlic. The dose for

children from 4 to 10 years of age is 0.10 grams oil of garlic and 10 drops oil of eucalyptus; for adolescents and adults it is 0.25 grams oil of garlic and 10 drops oil of eucalyptus. French investigators[12] recommend application on five successive days, to be repeated after an interval of three weeks. Garlic suppositories have no irritating effect on the rectal mucosa, and at the same time favorably modify the intestinal flora.

Deodorized garlic tablets at a rate of three daily for children, or six for adolescents and adults are prescribed for ten days each month over a six-months' period. Oral administration is supplemented by an enema of garlic in milk, nightly or every other night during the period the tablets are being taken[25]. Such a long drawn-out treatment, however, does not seem warranted in view of the quick and thorough results obtained with raw garlic. In one recent series garlic, raw or deodorized, led in 87 per cent of cases to a complete cure, a rate far better than that obtained from any other anthelmintic used[14]. The writer's experience confirms these findings. Garlic is routinely prescribed to combat pinworm infestation; the few patients who fail to respond are subsequently treated either with gentian violet or terramycin base.

Another common sense treatment for oxyuriasis has recently been reported by Dr. Bernard Landtman[17], of Helsingfors. Children received *bilberries* (huckleberries) in large quantities as exclusive nourishment for three consecutive days; when this medication was carefully supervised at a hospital, pinworms were completely eradicated.

The Problem of Reinfestation

Management of enterobiasis does not end with the destruction of parasitic organisms in the bowels of the host, but must also provide for the prevention of reinfestation. This may be brought on by transfer of infestive organisms from one part of the body to another (autoinfestation), or by contact with pinworm larvae in the patient's environment (heteroinfestation).

Autoinfestation is usually brought on by scratching of the perianal region with resulting transfer of pinworm eggs or larvae to mouth or nose. Terramycin ointment applied to the anal opening and perianal region will alleviate itching. The fingernails should be kept short, and cleaned daily. The hands must be washed frequently, especially after going to the bathroom, and before eating, always using a liberal quantity of soap and water, or still better, a detergent like Phiso Hex.

Other hygienic measures reducing the danger of transfer of pinworm eggs include: daily showers rather than tub baths; separate wash cloths for face and body; snug cotton drawers to be worn at night, and laundered daily. Sleeping clothes and bed linen must be aired daily, as sunlight will kill the eggs of *Enterobius vermicularis*.

It is much more difficult to render the environment noninfestive. Pinworm eggs have been found in house dust samples collected from all levels of a room, from the floor to the ceiling. Fumigation is no answer to the problem, as the embryos within the pinworm eggs survive exposure to hydrocyanic acid gas under conditions of commercial fumigation, and even exposure to stronger substances in controlled laboratory experiments[20].

Hygienic measures *by themselves* will not prevent cross-infestation. This was demonstrated by an experiment made at a girls' institution[7]. Rigid measures of personal and environmental hygiene were enforced during a period of six weeks, but at the end of that time the rate of infestation within the group had increased from 38 to 51 per cent! All the baking and boiling of toys, sterilizing of bedclothes, scrubbing of every object with which an infested child had come in contact, proved futile. Eradication of pinworms merely by hygienic measures is an impossible task, and elaborate instructions to parents on the subject of environmental hygiene, which in the end fail to produce the desired results, tend to discourage them from making sincere efforts to prevent reinfestation. The eradication of pinworms must be attempted on a family or institutional basis, but for that very reason a rational approach to the problem is required.

Measures of personal and environmental hygiene should never be suggested without concomitant prescription of specific medication. Furthermore, a procedure must be chosen which is practically feasible, and at the same time holds out the promise of cure within a reasonable period of time. There is no place in the treatment of enterobiasis for temporizing measures, as for instance repeated cleansing enemas. All members of the family should be examined as to the possible presence of pinworm eggs, and if necessary treated together as a group. If only one child is involved, he should sleep in a separate room for the duration of treatment. It is often easier to remove the child from the infested environment than to free the room in which he has been living, of all eggs and larvae. Even the most hardy eggs, however, will not survive over nine days in the absence of a proper host, and as a rule lose their infestiveness by the third or fourth day. A visit to grandmother's at the close of a course of treatment will often prevent reinfestation, and permit the eggs to die in the child's absence.

In recalcitrant cases in which reinfestation occurs in spite of medication and adequate hygienic measures, the possibility should be taken into consideration that the child might have become reinfested by contact with playmates. Occasionally control of oxyuriasis is possible only after the worm-filled appendix has been surgically removed[14]. Pinworms have been found in the appendix with increasing frequency[10,26], though *Enterobius vermicularis* is not etiologically related to appendicitis, and can be demonstrated more often in normal, or chronically inflamed organs than in those with acute inflammation[1]. Finally, it might be mentioned that pinworms have also been detected in Fallopian tubes, and even within the peritoneal cavity.

Summary

In his efforts to eradicate a relatively benign but extremely stubborn parasite, the clinician has employed vermicides which constitute a greater hazard to the patient's health than the parasite itself. Re-evaluation of the various preparations in common use is required in order to arrive at an integrated plan of management of enterobiasis. Lasting results will be obtained only if effective medication, the cost of which is not prohibitive, is combined with reasonable measures of personal and environmental hygiene. Prevention of reinfestation depends on recognition of the peculiar life cycle of *Enterobius vermicularis*. On the basis of a review of the literature and extensive personal experience a program is suggested for the simplified management of enterobiasis employing nontoxic anthelmintics.

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INTRACELLULAR BIOCHEMICAL ADAPTATION PROCESS THERAPY THEORY

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It is our concept that disease is the end result of an impaired mechanism that occurs within the cell and destroys the normal equilibrium within it. (Process Therapy Theory) Tuttle[1].

Selye's concept of disease[2] is expressed in his theory of the General Adaptation Syndrome in which he says that disease is a result of a "dysecretion of the pituitary gland or a dyscretive suprarenal cortex". "This may be stimulated glands giving rise to hyper-responses or it may be a depression of these glands and cause hypo-responses in the body."

This is expressed in three stages:

1. *Trauma:*—Myriads of traumatic agents act directly upon the target (body) and from the target area, they travel "some unknown pathway" to reach the pituitary gland which then produces a substance called the adrenocortico hormone. This stimulates the adrenal cortex to secrete hormones called corticoids.

2. *Adaptation Stage:*—The characteristic adaptive changes are in response to an alarm reaction and comprise nonspecific defense reactions. While these reactions are taking place, all the organs of the body show involutional or degenerative changes, "except the adrenal cortex, which seems to flourish on stress".

3. *Stage of Exhaustion:*—This is the state in which the acquired adaptation is lost.

The above can be summed up in terms of the Process Therapy Theory, and stated thus: Adaptability depends upon individual cellular activity and it starts immediately with the insult to the cell. Hence, based upon cellular energy potential, and intermediary cellular metabolism with its biological energy release, the General Adaptation Syndrome is governed[3].

This is graphically explained as follows:

1. Trauma:—The stage of alarm. Partial dephosphorylation > enzyme system breakdown > histotoxic anoxia > glycogen accumulation > pyruvic acid > fatigue.

2. *Adaptation stage:*—Phosphorylation reestablished via adenylic acid cycle (auto-defense mechanism) > enzyme formation > glycogen accumulation > pyruvic acid > lactic acid > oxygen > energy.

3. *Stage of exhaustion:*—Glycogen > pyruvic acid > glycogen > histotoxic anoxia > general fatigue > cyanosis > death.

The Process Therapy Theory

Impairment in the phosphorylation mechanism gives rise to pathology in the entire human system. Then, when equilibriums and balances are restored and maintained in the cells and tissues, body health is restored.

Cellular chemistry involves a harmonious series of consecutive steps brought about by a host of enzymes, all present in the same reaction fluid and the number, kind and amount of enzymes vary from one cell to another and determine the individuality of each cell. To discuss the function of the enzyme systems, one must first consider the formation of the chemical structure and the normal equilibrium of the individual cell. In the nucleus and cytoplasm of each cell, there are a group of compounds extremely important to the biochemical organism. One such compound—nucleic acid—consists of two types of nucleotides; pyrimidine nucleotides and purine nucleotides, which are held together by a phosphorylation mechanism.

Briefly, adenylic acid, adenosin monophosphate, adenosin diphosphate and adenosin triphosphate provide the battery of energy to the cell through the continuous exchange of phosphate radicals, which are donated in the utilization of glucose for the production of energy or for the synthesis of glycogen. In health, there is a continuous uninterrupted exchange of energy reversing this reaction. In disease the phosphate exchange is interrupted some place in the cycle.

All tissues constantly require the use of carbohydrates under all physiological conditions. Therefore, it is an indispensable fuel material, and whenever it is not available from food, it is made available by enzymatic synthesis at the expense of protein and fat. Carbohydrate is essentially similar in all tissues and organs, so that impairment in carbohydrate metabolism involves every structure of the body. The clinical symptoms that appear are merely the most obvious manifestations occurring in the tissues that suffer the most.

Carbohydrate serves not only as an important food, but as a part of the body's functioning machinery. It acts as a fuel; it has a protective detoxifying action, and it has regulatory influences on fat and protein metabolism.

Glucose enters the metabolic cycle of every living thing by the addition of a phosphate donated by adenosine triphosphate which hastens the breakdown of glycogen. The removal of the inorganic phosphate favors the synthesis of glycogen. The incorporation of inorganic phosphate has been observed to take place in the presence of living cells and high energy bond formation is a necessary preliminary for the oxidation of carbohydrate. Biological oxidation is limited by the extent to which liberated energy may be transferred to high

energy phosphate bonds. The final cellular oxidation of carbohydrate, protein and fat involves a catalytic cycle termed, "Krebs Citric Acid Cycle"[4] and requires specific enzymes and coenzymes.

Acetyl phosphate and oxalacetate are two substances that rise from the metabolic breakdown in the body of carbohydrate, protein and fat. Acetyl phosphate combines directly with oxalacetate and finally forms pyruvic acid. Other factors concerned in the citric acid cycle are co-enzyme A, formed from pantothenic acid, cocarboxylase (thiamine pyrophosphate), Ochoa's condensing enzyme[5], magnesium ions, and adenosine triphosphate.

Clinically, oxidation studies were made on a series of patients by determination of serum pyruvic acid which is one of the intermediary steps in the citric acid cycle. There is a rise in pyruvic acid above normal in the blood and excess quantities accumulate in the tissues of patients suffering from nutritional deficiencies, clinically manifested by symptoms of anoxia, particularly in those organs more severely affected. Yanof[6], demonstrated that there is an elevation, above normal (0.77 to 1.77 mgs.) of pyruvic acid in the blood of patients with heart failure, and this elevation approximates the degree of failure.

Our findings, confirmed by many others[7,8], bear further evidence that nutritional disease is a major etiological factor in metabolic disorders. In the majority of our cases, where these disorders were present, carbohydrate metabolism was profoundly disturbed as evidenced by changes in the chemical composition of the blood. Examination of the blood showed a rise in pyruvic acid, a fall in serum protein, and an elevation of cholesterol with a disproportionate fall in phospholipid.

The experimental work of Govier and Grieg[9,10,11], later supported by McGinty[12] and Bayley et al[13], demonstrated that lactate is the preferential carbohydrate substrate for heart muscle and that a breakdown in its metabolism is of importance in the viability of the ischemic cardiac cells. Lippman et al[14], established that the easily hydrolyzable phosphorus fraction, particularly adenosine triphosphate, plays an important role in the tissue transfer of energy. This compound continuously donates phosphoric acid radicals to the other metabolites, and this donation requires resynthesis continuum. In conditions of anoxia, therefore, the resynthesis of adenosine triphosphate would be impaired[15] and hence the content of easily hydrolyzable phosphorus is diminished. This chain of events resulting from such inhibited resynthesis of easily hydrolyzable phosphorus contributes considerably to the general pathological consequences of tissue anoxia. The observations of Weiss[16] and Haynes[17], support the author's view that cardiac manifestations depend on a faulty metabolism rather than a toxic effect of circulating metabolites.

In our cases of anoxia suffering from nutritional deficiency, the following are the general symptoms: Weakness, fatigue, nervous irritability, a history of nutritional deficiency commonly found with diets quantitatively high, but

qualitatively poor, constipation (usually spastic), flatulence, dyspnea with exertion, hypotension, more often than hypertension frequently with a compensatory tachycardia, cardiac enlargement, and angina pectoris.

In our patients, electrocardiographic changes denoting myocardial or coronary insufficiency were recorded when the electrocardiogram showed a prolonged P R interval, depression of the R S T segment over 0.5 mm. in any lead below the isoelectric line, and isoelectric or inverted T wave, except in lead three.

As the study progressed, it became increasingly apparent that the underlying biochemical dysfunction was a matter of lowered bio-oxidation. Greater emphasis was then given to stimulating intermediary metabolism.

Biochemical Approach to Chronic Progressive Diseases of Nutritional Origin

Atherosclerosis:—Atherosclerosis is an occlusive disease, and by progressively choking the blood supply, continues on to death. Large foam lipid cells under the epithelium encroach upon the calibre of the vessel. In time, secondary lesions become manifest; necrosis, hemorrhage and infarct[18].

The author[19,20], reported observations of 286 patients over a period of fifteen years who had a mean serum cholesterol of 300 mg. per cent, and a mean serum pyruvic acid of 2.3 mg. per cent. Hypotension was found in 153 patients, hypertension in 60, and normal blood pressures in 72. In 176 cases there was a relative leukopenia. It appears that, associated with hypotension, a paucity of leucocytes is a prevalent finding. Sabin[21] developed experimental evidence that leucocytic differentiation is related to oxygen tension. This depletion of leucocytes impedes the body's defense mechanism[22].

Tuttle[23] demonstrated that hypotension, with its reduction in coronary flow and disproportion between the available oxygen and the need or demand of the myocardium, is responsible for myocardial anoxia or coronary insufficiency. An inadequate oxygen supply is believed to be the primary cause of angina and of myocardial infarct.

Blumgart[24] found that the atherosclerosis is responsible for more than 90 per cent of patients with angina. He stated that skeletal muscles can borrow 30 per cent extra oxygen by their contractions. The myocardium, not able to do so, depends upon the oxygen immediately available. Any significant increase in demand by the heart requires immediate coronary increase in its flow, and that in reflex coronary vasomotor spasm, and in hypotension, the oxygen furnished to the myocardium is inadequate. It is this deprivation of oxygen to the myocardium that is the primary cause of angina and secondarily, there is a more or less ischemia which progresses to necrosis. On autopsy, he found that of over 90 per cent of angina deaths, there was a severe coronary

narrowing, and in all, the lesion contained an increase in the cholesterol and phospholipid content.

Gertler, et al[25,26] analyzed cases of one hundred patients under forty years of age who had definite coronary atherosclerosis. Biochemical studies disclosed that "the level of total serum cholesterol was higher in the coronary than in the control groups, and there was an overlapping between the two. This suggests that factors other than cholesterol play a role in atherosclerosis. By means of the partial correlation technic, it is shown that the serum phospholipids increase with age in both the coronary and normal groups. The degree of rise is proportionately less in the coronary than in the control group." Thus, he formulated the ratio of total cholesterol to phospholipid which gave a better indication of the biochemical status of the individual with respect to coronary heart disease than either serum cholesterol or serum phospholipid taken separately. The level of uric acid in the serum was greater in the coronary group than in the control[27]. It was found that by a formula incorporating serum uric acid, serum cholesterol and serum phospholipid that the value calculated was helpful in selecting patients predisposed to coronary heart disease.

Heuper[28,29] expressed the view that the colloidal stability of cholesterol in blood plasma, rather than in its concentration, is the significant factor in the genesis of atherosclerosis. Davidson[30] further found that most of the cholesterol in serum is not in free solution, but in colloidal form, stabilized by the phospholipids. Persistent and even transitory disturbances of the colloidal plasma equilibriums are therefore involved in human atherosclerogenesis. Gofman[31] describes serum lipid transport in terms of giant lipoprotein molecules. Almost all the chemical lipid components of serum can be accounted for quantitatively in the ultracentrifugally measurable lipoproteins. He describes them according to their flotation rates and molecular densities. He offers the hypothesis that the association of the S_f 12-20 and S_f 20-100 lipoproteins with atherosclerosis is strong, "although there is no direct evidence that these molecules are etiologic in the sense that they produce atherosclerosis directly by deposition in some manner from the serum." He considers the probability that the giant lipoprotein molecules provide a basis for prophylactic and therapeutic studies in atherosclerosis.

Based on my own twenty-two years of clinical and biochemical studies of atherosclerosis and on Gofman's Physics of Serum Lipoproteins, I offer a correlation of our own accumulated data.

Atherosclerosis, as evidenced clinically, is the result of a disturbance in the serum lipid transport. It is manifested both in the physical pathologic physiology as well as in the biochemical pathologic physiology, which occurs concomitantly. Biochemical studies reveal a significant disturbance in the ratio of these lipids which occurs probably simultaneously with changes in the physical molecular density and flotation rates of its molecules.

In biochemical physiology, as long as the rate of serum cholesterol and serum phospholipid rise proportionately, there appears little apparent clinical manifestation of atherosclerosis. This proportion is found true in the case of molecular physiology which Gofman describes thus: The lipoproteins represent a sequence of molecules involved in the normal metabolism of fat with progressive transformation of molecules of higher S_f classes into those lower S_f classes.

Atherosclerosis is manifested when certain pathological changes of macromolecules occur in the physical physiological processes. Increases in the quantity as well as increases in the number concentrates of the lipoproteins appear to be due to an abnormal rate of delivery of a particular lipoprotein to the serum, or to a partial metabolic block in the normal conversion of a particular lipoprotein to those of lower Sf classes. This consequence, likewise, is manifested when pathological biochemical changes occur in the proportionate rate of rise of serum cholesterol and phospholipid. It is when the serum phospholipid falls, that atherosclerosis appears clinically. All of these changes are insidiously progressive, as is indeed the deposit of their lipid elements into the arterioles.

Some investigators[32-35] are not in accord with the theory that atherosclerogenesis implicates a cholesterol-phospholipid relationship. A careful search through the literature failed to disclose an alternate thought or a concentrated study to fill the heretofore existing gap in our medical knowledge. Attention is directed to the vital statistics[36, 37] which continue to disclose that 51.3 per cent of deaths are due to cardiovascular renal disease. In the light of present knowledge, regulation of the blood lipids appears to offer the most promising approach to the problem of human atherosclerogenesis[38, 39, 19].

It has been reported by many other investigators that the serum lipids are significantly elevated in association with atherosclerosis[40, 41] and of particular significance is the demonstration of hypercholesterolemia in young individuals with coronary artery disease in whom no other factors contributing to the development of atherosclerosis were found[42, 43].

The products of faulty intermediary metabolism reveal themselves in an elevation of the cholesterol and pyruvic acid level in the blood. There is a relative lowering of the phospholipid which fails to hold the cholesterol in colloidal form. The latter then precipitates out of solution and deposits into the arteriolar endothelium, damaging its walls and impeding circulation. The structure most involved gives rise to disease characteristic to it. Involvement of the heart causes coronary disease; involvement of the brain, cerebral hemorrhage; inolvement of the liver, fatty degeneration which may progress to cirrhosis. We have always encountered an elevation in lipid metabolism simultaneously with an elevation in the pyruvic acid level. Since an increase in the level of pyruvic acid reflects an interference with oxidative mechanism

and also secondarily with phosphorylating mechanisms, we conclude that atherosclerosis is stimulated by imbalance in oxidative and phosphorylating mechanisms.

Obesity and its biochemical involvement:–The relative position of obesity, caused by endogenous or exogenous factors, is a moot question, variously expressed by many students of this subject. We found that emotional and endogenous imbalances play a most important part in the altered metabolism common to obese persons. In obesity, energy stored is greater than energy expended. The biological application of the physical phenomena is not quite that simple, for there are many conditioning factors to be considered. Because of their larger volume, obese people have a higher total metabolism than normal people. The laws of conservation of energy and matter apply here as do these laws apply universally.

In hypothyroidism and hypopituitarism there is a lowering of the basal metabolic rate and, hence, of energy requirement. Applying the law of conservation of matter, such individuals will gain weight if their caloric intake remains the same as before the endocrine disturbance developed. Clinically, many investigators report this to be untrue and note a hypothyroid leanness. From our own investigations[44], and in reviewing many such reports[45,46], the clinical distortion of the physical law appears to be due to a failure in measuring the individual's energy output. Obesity then, is not due directly to endocrine or obscure changes, but is the result of over-eating, relative to the individual's energy requirement.

Many reports express varied opinions concerning the relative importance of the etiological factors and the pathological consequences of obesity. Amongst these, in brief, is Newburgh's opinion[47], based on over-eating essentially, and on the complication of water retention in weight reduction. He observed carefully controlled hospitalized patients on a sub-maintenance diet and found that the patient actually lost fat tissue while the scale showed an increase in weight due to the retention of salt and water. Mossberg[48], in a study of over 500 children found that a constitutional, hereditary factor definitely exists and is common while Steiner[49], reported, "The primary factors at fault are largely psychological".

Since obesity adds a burden and disturbs the normal physiological functions of the body, it is a menace to good health. It is considered factual that excessive atherosclerosis accompanies the long standing obese state. We were able to establish an increase in total cholesterol and phospholipid in well over 500 obesity cases. In these patients who remained chronically obese, clinical symptoms of atherosclerosis and/or coronary insufficiency were manifested and the cholesterol phospholipid ratio was disturbed. This ratio was restored in most cases after corrective therapy was instituted and after normal weight was maintained. In the light of these findings, the determination of both serum cholesterol

and serum phospholipid and the evaluation of these figures is of utmost clinical significance in lessening the hazards incident to atherosclerosis through the control of obesity.

Gofman et al[50], using the physical phospholipid determinations, arrive at the same conclusion. To quote these investigators, "A positive correlation of atherosclerosis associated S_f 35-100 and S_f 12-20 lipoproteins with obesity provides part of the basis and possibly the largest part of the relationship of obesity with atheromatous vascular disease". They conclude, "Since many persons, after a loss of weight, show definite improvement in their Atherogenic Index values, the possibility of lessening the development of coronary atherosclerosis through the control of obesity is primary".

Effects of underfeeding producing nutritional deficiency states:—The effects of restriction of food energy have been thoroughly investigated. Such effects have been presented both in connection with widespread human starvation and in experimental studies[51]. There is a loss of weight, but a disproportionate skeletal growth persists[52]. Metabolic functions as measured by oxygen consumption show a diminution during persistent underfeeding[53], and the pattern of behavior adjusts itself to the restriction of calories. It would appear that under nutritional stress of this kind, the general slowing-up of activities represents the adjustments of the organism by eliminating the nonessential functions in order to preserve the integrity of the essential ones. A recent report[54] of the influence of the low caloric intake on certain of the endocrine systems supports this view[55]. Bontwell et al[56], observed that under experimental conditions of nutritional stress, the pituitary adrenal cortical mechanism was highly active, whereas there was a lowered secretion of the gonadotropic hormones as shown by the decrease in weight of the ovaries and uterus and the cessation of estrus. It appears that in conditions of undernutrition, emphasis is shifted away from hormone activity, which is required only incidentally, toward the endocrine mechanism which is essential to life.

Hypothyroid vascular disease:—For the maintenance of normal intracellular oxidation, an adequately functioning thyroid gland is essential. Any dysfunction that tends toward deprivation of thyroid secretion must be detected and treated early. Thyroid replacement must be administered judiciously under proper supervision to invigorate bio-oxidation. The biochemical indications for its use are, lowered serum protein bound iodine, an elevated serum cholesterol and an occult lymphocytosis. A low basal metabolism test is presumptive, while a therapeutic test is conclusive evidence of its need.

These factors are further emphasized in a paper by Kimball and Steiglitz[57], who stress that in the early recognition of hypothyroidism and its correction, lie the greatest preventive or anticipatory therapy. In a monograph by Kountz[58], it is stated, "One notes a greater occurrence of coronary thrombosis and intracranial hemorrhage in hypothyroid individuals who were not given thyroid". The

author presents evidence that a sustained and not a transitory hypofunction of the thyroid gland produces a degenerative change in the walls of the blood vessels and renders them susceptible to the development of atherosclerosis. To Tuttle's work, they add impressive support to the importance of accelerating oxidation as a means to retard degenerative processes.

Lange[59], had also shown that deficiency of the thyroid hormone as it occurs in hypothyroidism greatly increases capillary permeability, and this is reversed by administration of thyroid. Shapiro[60], and Steiner and Kendall[61], demonstrated that thyroid deficiency favors the development of experimental atherosclerosis, while the administration of thyroid, on the other hand, prevented its development.

Tuttle, in 1936, reported atherosclerosis, not as an inevitable process accompanying advancing age, but rather as a metabolic error, and as such, a preventable and reversible process. The results reported subsequently represent a twenty year period of degenerative vascular studies embracing more than a thousand patients. Whenever implicated, imbalances in other hormones, steroidal, sex, pancreatic, etc., are considered, as well as the thyroid. The incidence of these deficiencies and subsequent degenerative vascular disease is so great as to warrant their inclusion, at least as one of the major causes in the development of degenerative diseases. Temporary thyroid deficiencies are irrelevant and are not implicated in the production of vascular disease, but it is the slowly progressive, insidious results of insufficiencies that lay the foundation for subsequent degenerative disease.

In patients manifesting degenerative diseases who exhibit evidence of hypothyroidism, clinical improvement was obtained from adequate thyroid therapy. There was significant retardation of the degenerative process in treated patients, and a progression of degenerative changes in patients whose cooperation we failed to maintain. Morrison's later report[62], was in accord with ours, as was the work of Kountz and Chieffi[63].

Quoting Lawrence B. Ellis et al[64], they make this provocative statement: "Artificially induced myxodemia has been advocated for cardiac patients who have obstinate congestive failure or severe angina pectoris on the theoretic ground that the heart's work will be lessened because of the reduced metabolic rate of the body. But, since with myxodema, cardiac output may be reduced out of proportion to the drop in oxygen consumption, therapeutic hypothyroidism may have deleterious effects on the heart, outweighing the benefit of reduced metabolism." It was established that, regardless of age, hypothyroidism diminished cardiac output and increases the peripheral resistance in the circulation. Heart damage and circulatory insufficiencies are considered with cardiac enlargement and electrocardiographic abnormalities.

We found a general myocardial weakening with dilatation of both ventricles and symptoms manifesting cardiac insufficiency. The electrocardiographic changes commonly found are: (1) bradycardia; (2) low voltage of all complexes;

(3) depression of the ST segments and (4) T wave approaching the ilsolectric line, on or below it. The electrocardiogram affords valuable guidance in the regulation of thyroid dosage. We correlate the electrocardiographic findings, with the biochemical pathologies and can report that a restoration towards normal in the serum chemistry with biocatalysts is followed after a short lag in time by a restoration towards the normal in the electrocardiograms.

The pertinent serum pathologies concerned are elevation of the total cholesterol and phospholipid with a disturbance in their ratio, elevation of pyruvic and of uric acid, a lowered serum protein and a lowered protein bound iodine. In addition, a complete blood count and a lymphocytic index yielded more important information.

In only thirty cases, we recorded ballistocardiographic tracings, but these are too few for a statement now, which we hope to report in the future. At present, it may be suggested that the ballistocardiograph appears to be an aid as a recorder of coronary insufficiencies sometimes producing positive findings, when the electrocardiogram is borderline.

It is interesting to note that whenever serum pyruvic acid is beyond 2 mg. per cent, lipid metabolism is disturbed, electrocardiographic tracings are proportionately pathological and, generally, uric acid is elevated and the serum protein bound iodine is low. This is pathognomic of hypothyroid-vascular disease.

Our studies into the biochemical effects of faulty oxidation advances the belief that all gross and minute morphological, pathological and physiological changes are indicative of disarrangement in the cellular biochemical patterns. The retarded metabolic oxidation tends to accelerate the degenerative processes through disturbances of the plasma colloids such as cholesterol and phospholipids. This is subsequent to faulty carbohydrate metabolism up to and below the stage of pyruvate.

The essential restorative measures that comprise the stepping up of aerobic and anaerobic oxidation are as follows:

1. Thyroid administration, which accelerates intracellular oxidation. The dose is increased to within the individual's tolerance to the drug. Its activity is reflected in cellular differentiation, expressed by selective increase in mesodermally derived lymphocytes.

2. Administration of vitamins, particularly Vitamin B in proper formulation as suggested by Cayer[65], is used to accelerate intracellular respiration. A preparation containing the oxytropic factors of the B-complex group, cocarboxylase, (phosphorylated thiamin) yeast enzymatic hydrolysate and divalent minerals is employed to restore enzymatic interplay and to correct carbohydrate metabolism.

3. A proper dietetic regime. The deprivation of certain fats and other high cholesterol foods is required in a therapeutic diet to restore lipid equilibration[66].

Animal sources of cholesterol and of nonphysiological fats are excluded in order to lessen the work of liver. The more the fat is hydrogenated, the harder it is for the liver to desaturate it.

Vegetable oils which contain phytosterol, are included because they are not used in the human economy. The iodine number of these oils is high, therefore, this lipid is correspondingly highly unsaturated. It relieves the liver of the desaturation burden and helps in the utilization of free cholesterol. Protein and carbohydrates must be biologically adequate and are important stimulants of the oxidative processes.

Dietary restriction of cholesterol has been deprecated on the bases that its restriction eliminates only the exogenous quota, while the endogenous quota is much higher than provided by a normal diet. Such reasoning appears fallacious because of its incompleteness.

The restriction of cholesterol foods alone will be helpful but will not completely control this metabolic disorder any more than restriction of sugar alone will be helpful but will not completely control the diabetic metabolic disorder. In the former disease, acceleration of hepatic activity by lipotropic agents and thyroid is required. This analogy also applies to gout. Dietary restriction alone of purine will be helpful but will not completely control this metabolic disorder in which serum elevations of both cholesterol and uric acid are involved. The lipotropic agents are lecithin, choline, methionine, inositol and lipocaic. They are used to facilitate the transporting of fat from the liver whether that deposition of fat is the result of an increase in the rate of fat supplied to the liver, or due to a decrease in the rate at which the liver is able to dispose of fat.

Cognizance is taken of the fact that many of our patients were treated with more than one therapeutic approach or agent. Associated disorders were prescribed for as indicated. The hematopoietic agents and hormones were prescribed when necessary. In addition, temporary measures for the relief of muscle spasm and nerve irritation were taken for control of pain resultant from osteoarthritis[67], which is essentially a joint manifestation of hypothyroid-vascular disease and was treated as such.

In conclusion, we may state that the treatment of hypothyroidism and its associated disorders is predicated on the replacement of the process biocatalysts and the clinical results bear further evidence substantiating the Process Therapy Theory[1].

Biochemical derangements of the pancreas:—The diagnosis of pancreatic disease and the differentiation of its lesions are largely dependent upon the biochemical studies of the concentration of pancreatic hormones and enzymes. The hormones involved in this endocrine gland are insulin, which lowers blood sugar and the hyperglycemic-glycogenolytic factor (H.G.F.) that raises blood sugar and the enzyme amylase, the carbohydrate splitting enzyme, and lipase,

the fat splitting enzyme. Amylase, found in the blood, originates not only in the pancreas, but also from the salivary glands. Bruschwig[68], gives clinical evidence in support of the experimentally demonstrated fact that the pancreas or the salivary glands are not the sole sources of amylase production. After total pancreatectomy, the serum amylase in his patients fell to nine units in one week postoperatively and rose to a normal 71 units eight weeks later.

In 1929, Elman[69], demonstrated that acute pancreatic duct obstruction results in serum amylase elevation. Blood amylase rises in the first hour of pancreatic affection, reaches a maximum in twenty-four hours and then falls to normal by the 72nd hour of illness. Thus a primary elevation may be missed, and therefore, a normal amylase does not explain pancreatic disease. Even an elevated blood amylase may not be taken as an absolute indication of pancreatic disease. Dreiling[70], states that blood amylase elevations, when present, are valuable in confirming a diagnosis of acute pancreatitis, otherwise the results of blood amylase tests are inconclusive since serum amylase may also occur in acute cholecystitis[71], choledocholithiasis[72], biliary dyskinesia[73], and penetrating duodenal ulcer[74].

Malinowski[75], strongly favors serial serum amylase tests as a guide in the diagnosis of acute pancreatitis and in the acute exacerbations in chronic recurrent pancreatitis, and he recommends that serum amylase determinations be made routinely in all patients with acute abdominal pain. Elevated amylase in such patients invariably is of diagnostic value when correlated with other clinical findings. Clinical evaluation of serum amylase enhances the diagnostic importance of the test.

Dreiling[76], however, favors the secretin test. It yields quantitative data of pancreatic secretions by examination of the duodenal drainage following secretin stimulation. It is invaluable in the detection of pancreatic insufficiency in chronic diseases of the pancreas. Its value in diagnosis of acute pancreatic disease is limited by the rapidity with which the pancreatic secretion returns to normal range. In the advanced stages of both diseases, these responses are no longer diagnostically distinct. He favors a combined secretin-pancreozyme test which he hopes will resolve the prevailing difficulties for the study of pancreatic secretions.

Evidence suggests that H.G.F. functions physiologically. It is derived chiefly from pancreatic alpha cells, and also from gastric and duodenal mucosa. It elevates blood sugar by causing a liberation of glucose from the stores of liver glycogen. Pincus[77], demonstrated that when the hepatic glycogen stores are depleted, as after a 72 hour fast, injection of H.G.F. results in only a minimal rise in blood sugar. Sutherland et al[78], studied the mechanism of H.G.F. on liberation of glucose from the liver and found that a hepatic phosphorylase is activated.

Observations in humans have led to results that suggest a pancreatic factor other than insulin influences metabolism in health as well as in disease. It seems

significant that a diabetic patient who must have a total pancreatic excision, often requires less insulin after surgical intervention. Apparently, the duodenal and stomach mucous membranes, probably by way of their alpha cells, are stimulated to greater functioning of the hyperglycemic-glycogenolytic factor. Brunschwig[79], reports that a number of his patients are still significantly free of indigestion nine years after pancreas was excised. His contributions add further support to the evidence that mucous membranes of the duodenum and stomach are stimulated to increase activity in a compensatory manner.

Warburg[80], points out that malignant tumors may be regarded as anaerobic parasites which compete and encroach on normal tissues by a superior utilization of glycolytic energy for their life and growth. Of great clinical significance is the fact that whenever a progressively severe diabetic is beginning to require less insulin, one may suspect the presence of cancer.

Insulin is actually a biocatalyst which acts by influencing other biocatalysts. The fall in the blood sugar level is a direct reflection of the influence of insulin on the basic phosphorylation, and the association of potassium with the hexose phosphates in muscle, also accounts for the withdrawal of blood potassium.

With the anoxia associated with diabetic acidosis, there is a reduction in the serum potassium concentration. The factors that combine to produce this reduction are: (1) loss of potassium in diuresis and dehydration with resultant loss of intracellular stores of water and potassium; (2) loss of potassium as a result of inadequate insulin.

As early as 1937, the author reported that cardiovascular complications in diabetes were found to be the direct result of lipid metabolic dysfunction and, in addition, that endocrine imbalances also play an important part in the cause and course of diabetes. The pituitary and suprarenal glands were particularly implicated. In the years following, these facts have been established and elaborated upon.

Biochemical processes in diabetes:—Diabetes mellitus is a metabolic disorder in which carbohydrate metabolism is profoundly disturbed. The growing knowledge of the hormonal systems has enhanced our understanding of, and is crucial to an approach to the treatment of diabetes mellitus.

In terms of organ functioning, the liver is the prime factor for the maintenance of the normal blood sugar level. Once sugar has entered the peripheral tissues, even though it is stored rather than used, it cannot reenter the blood as glucose, except during periods of relative muscle anoxia, when lactic acid is carried to the liver, converted into glycogen, and reappears as blood sugar (lactic acid cycle).

Diabetes is considered to be a disease of glucose overproduction in which there is no diminution of the utilization of blood sugar by the tissue, but the

supply of sugar to the blood by the liver has become excessive to the point where continued normal utilization can no longer keep pace with it.

The ketone bodies, so frequently associated with severe diabetes, are normal intermediates of fatty acid catabolism in the liver and they appear in excess in the blood when the hepatic metabolism of fat is sufficiently increased by the lack of carbohydrate. The ketone bodies are readily utilized by the peripheral tissues under all known conditions. The liver is practically the sole source of origin for ketone bodies appearing in the urine. In a diabetic forced to metabolize fat, the liver forms these substances at a much greater rate than it can metabolize them.

Not a single hormone has been discovered which has not been shown to exert some influence on carbohydrate metabolism, by virtue of catalytic effects on the enzymatic machinery of metabolism. Insulin is the most effective of all known hormones in relation to blood sugar level. With insulin hypoglycemic effects are invariably obtained, regardless of age, state of nutrition, or of the presence or absence of various endocrine glands or visceral organs, and this effect of insulin is a general one and not mediated by any particular organ or tissue. Blood sugar lowering from insulin is primarily the result of the more rapid withdrawal of sugar from the blood by other tissue and secondarily the result of decreased supply of sugar from the liver to the blood.

Liver

The liver is the central organ of intermediary metabolism and a regulator of digestive and tissue exchange. The "heterogenisity" of its functions are well classified by Weiss et al[8].

Metabolism of carbohydrate:—The breakdown of glycogen to glucose in the liver is termed hepatic glycogenolysis and is the result of phosphorylysis and hydrolysis by the enzymes phosphorylase and a glucose phosphatase found only in the liver. The liver cells do not contain the active glycolytic enzyme system which breaks down glucose and glycogen to lactic acid. This system is found in the general tissues and requires phosphorylation reactions which catabolize glucose and glycogen to lactic acid, and which escapes from the tissues into the blood where most of it is transported to the liver. The liver then converts the lactose to glycogen and is restored back to the blood and tissues as glucose. Under conditions of stress, the liver glucose may be spared at the expense of muscle glycogen via the lactic acid cycle. When adequate carbohydrate is available, hepatic glycogenolysis is slowed up. This important property acts to spare the catabolism of protein and fat which has valuable nutritive significance. Adequate carbohydrate energy prevents the breakdown of fat to ketone bodies and constitutes the antiketogenic activity.

There are three phases of carbohydrate metabolism in man. These are glycolysis, its anaerobic phase; oxidation, its aerobic phase and the phosphorylation phase upon which both are initially dependent.

Metabolism of protein:—Enzymes contained within living cells have a property of synthesizing proteins from amino acids and have specific properties in accordance with the character of the cell. To accomplish synthesis, energy from the catabolism of carbohydrates is required. Abnormal proteins occur only in the presence of dysfunctioning cells. Normally, amino acids are continually assimilated and liberated by the tissues in which the liver is especially active. Under conditions of protein starvation or general malnutrition through dietary failure or liver cell damage in toxemia, hepatic synthesis fails and hypoproteinemia results, then the cells yield their protein to supply energy. The preservation of normal plasma protein levels is one of the important functions of the liver since it is the plasma proteins which act as vehicles transporting nutritive and blood cellular elements to the tissues.

There are ten amino acids which are necessary for the maintenance of nitrogen equilibrium that must be provided through dietary proteins as these cannot be readily synthesized by the liver and since they are required, are called essential amino acids.

Not only does the liver function in the resynthesis of proteins from amino acids and in the maintenance of plasma tissue protein balances, but it is the important organ concerned in deaminization in which the nitrogenous component of its molecule is excreted as urea and the remaining part is converted chiefly to glucose with a fractional amount as fat.

Metabolism of fat:—The liver is the most important organ concerned in the intermediary metabolism and the transport of fats. It forms the bile salts, unsaturated fatty acids and produces phospholipids from the neutral fats. Under normal conditions the liver does not store fat, but it does so under pathological conditions which result in the impairment of liver functions and degeneration in the cells. When the metabolism of fat is sufficiently increased by the lack of available carbohydrate or protein, ketones appear in excess. Fatty livers produce much greater amounts than normal livers as an intermediate of fatty acid catabolism. Under physiologically functioning conditions there is a continuous mobilization of fats into, and a transport of fats out of the liver. The phosphorylation mechanism is the means by which these metabolic processes occur. Determination of the amount of fats in the plasma is of clinical importance and is used as a means for detecting susceptibility towards atherosclerosis and its related conditions. An increase in plasma fat content may be the result of dietary excesses or an oversupply from fat depots which occurs during starvation, or it may result from a damaged liver unable to dispose of fat at a normal rate. Such excess may then be deposited into and damage the body cells. This may cause an hepatic circulatory insufficiency and progress to cirrhosis of the liver with impairment in all of its functions.

The normal liver is believed to contain an excess of phospholipid greater than neutral fat, but in fatty degeneration the neutral fat which has a very low iodine number is in excess. There is a large scale and long enduring demonstra-

tion that a relation exists between the nature and the amount of lipids ingested and hypercholesterolemia in certain diseases as atherosclerosis, associated with it. This condition as explained on a basis of diet by Pacini, has furnished a constructive biochemical comparison of the blood studies of native Chinese in China and of native Americans in the United States as follows:

TABLE I

Lipid	Native Chinese	Native Americans
Iodine number of blood fats	130-180	80-115
Blood Cholesterol mg./100 c.c.	90-120	150-220

The iodine number measures the sum of iodine atoms that attach themselves to the free unsaturated linkages in the fatty acids and lipids, and is defined as the per cent of iodine attached.

A comparative study was made of a family of five Chinese siblings, all born in China. Three came to the United States at an early age. Two died of coronary atherosclerosis, diagnosed clinically and confirmed by autopsy, while the two who remained in China were alive and well.

TABLE II

Sib.	Place	Age	Iodine Number of Blood Fats	Cholesterol mg./100 c.c.	Result
1	China	63	172	108	Well
2	China	67	168	94	Well
3	America	56	105	360	Coronary
4	America	58	99	310	Coronary
5	America	52	127	280	Lost to study

These significant differences are explainable by diet intake which, in the case of the Americans, contains considerable quantities of low iodine number of saturated hydrogenated fats while the Chinese diet, on the contrary, is predominantly free of all hydrogenated fat, but consists of considerable quantities of unsaturated high iodine number of fatty acids containing lecithin, derived particularly from soy bean. In adequate amounts, the lecithin acts as a colloidal stabilizer.

Lipotropic agents:—Specific lipotropic agents such as inositol, choline, lecithin, methionine, protein and lipocaic as well as certain vitamins as the B-complexes, ascorbic acid and Vitamin A are necessary food substances used to facilitate the transport of fat from the liver. They aid in the restoration of malfunctioning liver cells towards the normal.

The principal lipotropic concerned appears to be lecithin, a phosholipid in which choline is the nitrogenous base. Under conditions of inadequate choline, it is synthesized from the labile methyl group liberated from methionine, an essential sulfur-containing amino acid. In addition to entering into the synthesis of choline, its labile methyl group is utilized in the metabolism of phosphocreatine, necessary for muscle energy, and it has active hepatic detoxifying properties. Inositol and lipocaic are required to prevent specific types of fatty infiltration of the liver and to promote phospholipid synthesis. Lipocaic is the lipotropic hormone of the pancreas and it is its inositol content, a member of the Vitamin B group, to which it owes this property. To maintain normal liver lipid metabolism and to prevent or treat degeneration, dietary lipotropic agents, adequate utilizable carbohydrate and liberal protein are required. In chronic diseases of the liver, there is a disturbance in the erythrocyte factor and antipernicious factor and in its normal storage of iron and copper. This accounts for the difficulty in correcting anemia caused by liver disease until the liver function is restored, and folic acid and Vitamin B_{12} contribute towards its correction.

Steroid Hormones

Steroid hormones are believed to influence metabolic processes by their effect in the living system on cellular energy transfer and its consequent transformation of matter. This means they must effect, by their excess or withdrawal, imbalances in carbohydrate, fat and protein metabolism. They act on enzyme activity, therefore they affect metabolic equilibria and reaction rates. These hormones exert their action as chemical regulators through modifying some link in the chain of metabolic reaction, i.e., the sex hormone's effect on weight gain or loss of testosterone propionate. Estrone is believed to inhibit oxygenation of fats. Gyorgy et al[81], demonstrated the effect of ethenyl estradiol in preventing fatty degeneration of the liver by its lipotropic activity and influence on oxidation of fat metabolism.

Equilibria or antagonisms between steroid hormones cover a large and very interesting field. Such equilibria or balances exist throughout the entire human system, i.e., avidin-biotin, purines-pyrimidines, hyperglycemic-glycogenolytic factor-insulin, cholesterol-phospholipid, calcium-phosphorus, albumin-globulin.

By the steroidal equilibria, it is demonstrated that one steroid hormone will diminish the action of another compound by preventing, directly or indirectly, its metabolic effect. These balances, for example, are estrogen and progesterone[83]. Excess estrogen suppresses pituitary secretion, while depressed estrogen levels increase it. When the genital organs cease their function and the adrenal glands become the source of supply for estrogen and androgen, pathological conditions may result. The withdrawal of ovarian or testicular secretion permits an increased or unchecked action of the pituitary gland, stimulating the output of minerolocorticoids and glucocorticoids. Such conditions as cardiovascular disease may be intensified by the deposit of hyalin through the excess production

of minerolocorticoids, while osteoporsis and diabetes are diseases that may be accelerated from excess production of glucocorticoids.

Treatment with steroid hormones has a wide scope in its effects on body activity[84]. Administration of cortex or the androgens favors the retention of nitrogen, phosphorus, potassium, sodium and chloride and causes an increase in urinary 17-ketosteroids. In the androgenital syndrome, laboratory determination of the 17-ketosteroids is of great diagnostic importance. These compounds act on intermediary metabolism to increase blood sugar and liver glycogen, catabolize protein to carbohydrate, aid in fat transport from its depots and cause an increase in urinary uric acid with a lowering of urinary creatinine.

Summary

Employing the biochemical blood values as indicators of the biochemical dysfunctions associated with pathological conditions, it is endeavored to postulate the Process Therapy Theory as to the etiological factors responsible for the chronic progressive diseases of nutritional origin.

Clinical experience, supported by blood biochemical studies, are presented to throw further light on the pathology of atherosclerosis, and the factors which may be the precursers of its origin. That atherosclerosis in the young may be reversible when detected early is indicated. The liver and pancreas are shown to exert influence on cellular metabolism.

Biochemists are in general accord in the belief that steroid hormones act indirectly on the metabolic processes by their direct influence on the enzyme system. Their catalytic properties are by way of effecting the rates of transfer of energy and their role as chemical regulators in the intermediary cellular metabolic oxidations is a major function.

The equilibria are maintained, in the author's estimation, by the phosphorylation mechanisms resulting from the adenylic acid systems and directly to nucleic acid. Therefore, the Process Therapy Theory holds the key to the factors at fault since it is concerned with the equilibria and properties of living cells composing the tissues and organs of the body as it relates to growth, maintenance and repair of the living body as a whole.

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A PRELIMINARY STUDY OF THE THERAPEUTIC ACTION AND TOXICITY OF AN ANTICHOLINERGIC (3-DIETHYLAMINO-1-CYCLOHEXYL-1-PHENYL-1-ETHIODIDE)*†

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Introduction

In animals 3-Diethylamino-1-cyclohexyl-1-phenyl-1-ethiodide, for brevity hereinafter called Pathilon, has been shown to have an anticholinergic action of greater magnitude and wider therapeutic range than Banthine[1]. When given to dogs for periods up to three months and to mice for one month, it has been shown to have relatively little toxicity[1]. Acute toxicity is also low[1]. Because of this low toxicity and the demonstrated anticholinergic action, it was decided to try the drug in human beings to test both its toxicity and its possible therapeutic usefulness in gastrointestinal disorders.

Procedure

Sixty-six patients were selected from the gastroenterological and medical clinics of the Welfare Island Dispensary, a unit of the New York Medical College, as well as from private practice, for the study of Pathilon. Of these, 51 were gastroenterological cases and were studied for therapeutic effects as well as for side-reactions. The remaining fifteen were general medical cases, selected at random and were studied mainly to observe any toxicity resulting from the administration of the drug. The medication was given in daily doses ranging from 30 to 375 mg. The patients returned weekly to the clinic during periods of observation, ranging from one to twelve weeks. In this preliminary study, all symptoms were recorded and new symptoms analyzed for their possible relationship to the action of the drug. All subjects were told to follow their usual diets and no change in their habits was advised. They were not given any antacids or antispasmodics or sedatives.

As utilized in this study, the terms marked improvement, slight improvement and no improvement may be defined as follows: by marked improvement we mean complete control of the symptoms during the period of administration of Pathilon; by slight improvement is understood that a significant regression of some one or all of the symptoms was observed; the term no improvement is self-explanatory.

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*The drug and a placebo were both furnished to us through the courtesy of Dr. J. M. Ruegsegger of the Lederle Laboratories, under the trade name Pathilon.

†This work was done in conjunction with the New York Medical College, Metropolitan Hospital Research Unit, Dr. Thomas H. McGavack, director and the Department of Medicine, New York Medical College, Dr. Linn J. Boyd, Professor and Director.

A placebo identical in physical appearance with the medication was given to a significant number of patients. All patients were discarded from the study as being unreliable in whom placebo favorably altered symptoms or produced numerous new manifestations.

TABLE I

THE RESULTS OF TREATMENT WITH ANTICHOLINERGIC DRUG PATHILON

Diagnosis	Number of Patients	Daily Dose (Mg.)		Duration of Treatment (weeks)		Results			Side-effects	
		Range	Aver.	Range	Aver.	Great Imp.	Slight Imp.	No Imp.	No. Times Occurring	Manifestation
Gastritis	26	30-375	78	1-12	4	5	12	9	11	Dryness of mouth, etc, "tight" stomach
Duodenal ulcer	14	30-150	45	0.5-12	6	10	3	1	3	"Hot" stomach; Dryness of mouth.
Gastric ulcer	4	30-225	66.6	4-11	8	3		1	2	"Hot" feeling in stomach (150 mg.) Dryness of mouth (30 mg.)
Marginal ulcer (subtotal gastrectomy. gastric ulcer—1944)	1	30-150	90	4	4	1			0	
Postcholecystectomy syndrome	2	30-75	45	2-4	2		1	1	0	
Gastric malignancy	1	75	45	1	1			1	1	Increased epigastric pain
Spastic duodenal bulb	1	30-75	51	4	4	1			0	
Irritable colon	1	30-150	84	5	5		1		1	Dryness of mouth, "bloated" stomach (150 mg.)
Necator Americanus infestation	1	30-150	96	7	7		1		1	Increased ep. pain (60 mg.) Decreased ep. pain (150 mg.)
TOTALS	51	30-375		5-12		20	18	13	19	

RESULTS

The results of treatment in these 51 patients are summarized in Table I.

I. *Therapeutic action in gastrointestinal diseases:*—In this group of 51 patients, there were 26 who were classified under the broad heading of gastritis, 3 of which were alcoholic. As a group these 26 individuals complained

of epigastric pain, heartburn, gaseous eructation, nausea and vomiting and showed no intrinsic gastrointestinal lesion demonstrable by roentgenographic study following a barium meal and enema. There were 19 cases of peptic ulcer of which 14 were duodenal, 4 gastric and 1 marginal. There were 2 patients with the "postcholecystectomy syndrome" and one each with gastric malignancy, irritable colon, spasticity of the duodenal bulb and infestation with necator americanus. Each of these complained of epigastric pain and heartburn.

TABLE II

SIDE-EFFECTS OF PATHILON IN 66 PATIENTS

No. of Patients	Age		Dosage (Mg.) Total				Dis'n to No. of Patients	Total Side Reactions	Cramps in stomach	Tight stomach	Inc. epigastric pain	Bloated stomach	Burning of stomach	Constipation	Dizziness	Sleepiness	Dist'd Resp.	Dry mouth, tongue	Urge to Defecate	Visual Dist.	Nervousness
	Range	Aver.	Unit	Daily	Range	Aver.															
32	23-61	42	10	30	60-180	120	1: 60 1: 90 11: 20 19: 180	4	1					1		1					1
11	34-59	37	20	60	360	360	11: 360	3		1								1			1
27	35-55	45	25	75	300-450	375	6: 300 21: 450	2				1						1			
1			30	90	180	180	1: 180	0													
2			40	120	480	480	2: 480	0													
30			50	150	600-900	800	8: 600 22: 900	11				2			1		1	6	1		
13			75	225	450-1350	900	2: 450 8: 900 2:1350	4		1	1			1			1				
5			100	300	600-1800	900	2: 600 1:1200 2:1800	4					1					2		1	
2	52-55	53	125	375	750-2250	1550	1: 750	2						1	1						
							1:2250														
123							Total	30	1	2	1	3	1	3	2	1	2	10	1	1	2

In the case of the duodenal ulcer which showed no improvement, a subtotal gastrectomy was subsequently performed for an ulcer which had penetrated deeply into the pancreas.

In connection with this study, it was generally known that many patients showed significant improvement on as little as 10 mg. of Pathilon three times daily. It was equally clear that after improvement was not attained with 25 mg.

doses three times daily, it was also unlikely that higher dosages would be effective. Inasmuch as signs of toxicity are more or less absent until a total daily dose of 150 mg. is reached, this affords us a toxicity-therapeutic ratio (therapeutic index) of two.

II. *Toxic effects of (anticholinergic drug) Pathilon:*—As was stated above all 66 patients were observed for any toxic action of Pathilon; 51 for therapeutic as well as side-effects and 15 primarily for the detection of any untoward action. In this latter group were included 4 cases with neurasthenia, 5 with menopausal manifestations, 3 with generalized arteriosclerosis and 1 each with chronic bronchitis, bronchial asthma and paroxysmal tachycardia. The patients were at first given 10 mg. of Pathilon every 8 hours. This was increased later to 25 mg., then to 50 mg., and finally, in some cases, to as much as 125 mg., every 8 hours. These subjects returned to the clinic at weekly intervals, where new symptoms, all subjective complaints and physical status were carefully appraised.

The most commonly encountered untoward symptom was dryness of the mouth, tongue and/or throat. This occurred with the administration of about 150 mg. of Pathilon daily. The other toxic symptoms in the order of frequency were "bloated" stomach, constipation, dizziness, "tight feeling in the stomach", difficulty in catch the breath, nervousness, abdominal cramps, sensation of something in the eyes, sleepiness increased epigastric pain and "burning" in the stomach. These complaints were relatively infrequent and are summarizd in Table II. While it is possible that some of these symptoms were not directly due to the action of the drug, all reasonable precautions were taken to eliminate from the study those patients who were unreliable in recording effects. This was done with the use of a placebo and as a result of this care, 14 patients were discarded either at the beginning or after some treatment had been given.

From inspection of Table II, it will be noted that the incidence of side-effects increased abruptly with unit doses of 50 mg. and total doses daily of 100 mg. Below this point, we consider the drug nontoxic.

Summary and Conclusions

Pathilon was administered to 66 patients, 51 of whom were suffering from gastroenterological complaints and 15 were general medical cases selected mainly for toxicity studies. The daily doses ranged from 30 to 375 mg. for periods of from one to twelve weeks. Twenty of the gastroenterological patients, 13 of which were peptic ulcer cases, showed great relief, 18 had slight improvement and 13 had no improvement. In the toxicity studies of all the 66 patients, 10 complained of dryness of the mouth, throat and tongue, when the dosage was increased to an average of 800 mg. a day. Other untoward symptoms are as listed.

REFERENCE

1. Personal communication from Drs. B. K. Harned and R. W. Cunningham of Lederle Laboratories.

POSTGASTRECTOMY GASTRITIS

BERNARD J. FICARRA, M.D.*

Roslyn Heights, N. Y.

The lowered mortality in gastric surgery has increased the number of patients subjected to gastrectomy for the treatment of certain lesions of the stomach and duodenum. It is not the purpose of this discussion to present the indications for gastrectomy or to evaluate the procedures of choice in gastric surgery. It is our intention rather to recall a postgastrectomy pathologic state which is often over-

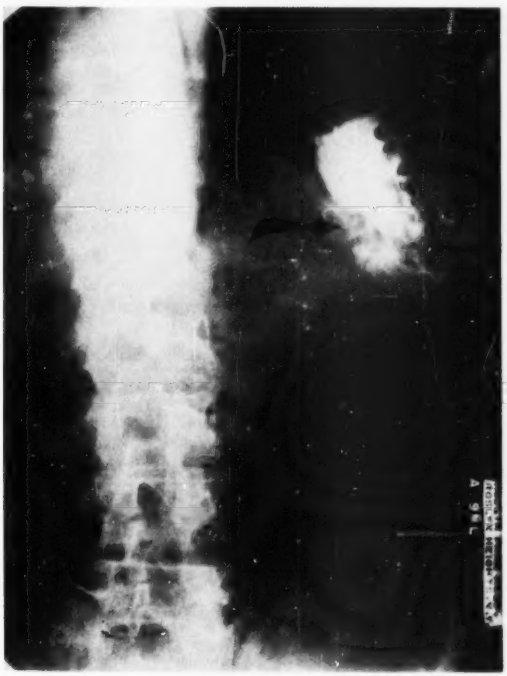

Fig. 1—Postgastrectomy gastritis due to a "too small" stoma. The gastritic process is more pronounced and more localized at the stoma.

looked when a patient fails to secure the anticipated beneficial results following gastric surgery.

Attention at this time is focused upon postgastrectomy gastritis or as it may sometimes be termed "stump gastritis". Both these terms refer to gastritis developing in/or persisting in the residual proximal stomach following gastric

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resection. This pathologic condition may have existed before operation or developed following gastric surgery. In either event it is often given minor consideration, or not thought of, when a patient fails to enjoy the expected beneficial results following gastric surgery.

Clinical Picture

Postoperative gastritis may give no immediate symptoms or may produce an immediate serious one such as hematemesis. The first indication that all is not well following a gastrectomy may be that the patient does not feel that the operation has completely relieved him of his complaints.

Fig. 2—Postgastrectomy gastritis of the hypertrophic type. In this x-ray it is more marked on the greater curvature above the anastomotic site.

These minor complaints may be epigastric discomfort which the patient may describe as a sense of pressure or the "feeling" of fullness after meals. The major complaints may be cramp-like pain or distention developing soon after meals. Often these symptoms are aggravated by a change in posture or by exertion.

Rarely does the patient complain of vomiting, constipation or diarrhea. When diarrhea is a sign, thought is given to the possibility that the patient may be developing a gastrojejunocolic fistula.

The most serious of all complaints is hemorrhage. It is probably true that gross bleeding in patients with an early gastrojejunal ulcer is bleeding from gastritic erosions. Massive hematemesis can occur in severe "stump gastritis". On one occasion a patient developed such severe hemorrhage that a second operation was imperative (seven days following subtotal gastrectomy for peptic ulcer). The anastomosis was disconnected and the gastric mucosa examined. The entire mucosa was oozing blood and the appearance was that of an acute hemorrhagic gastritis. This young male patient expired. The possibility of "stump gastritis" following gastrectomy should be considered among other causes when there is a persistence of preoperative symptoms. Gastroscopic examination and x-ray studies will assist in arriving at a proper diagnosis. By excluding the presence of a recurrent peptic ulcer it is most likely that the presence of any of the symptoms mentioned above may be due to gastritis.

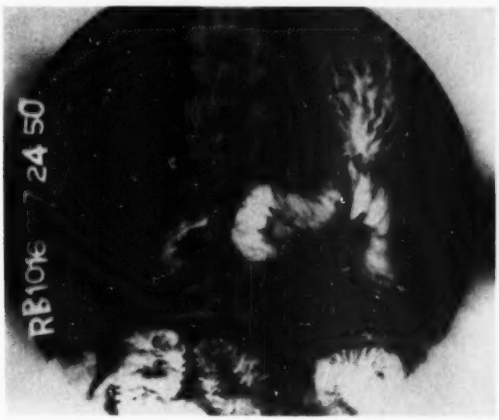

Fig. 3—Postgastrectomy x-ray showing an involvement of the entire residual stomach with "stump gastritis".

Etiology

It is doubtful that one factor alone should be indicted as the cause for "stump gastritis". Nevertheless one factor may be the precipitating cause. In those cases where gastritis has been present prior to operation, it is highly probable that the trauma of operation has in some way affected the blood supply which results in an exacerbation of, or increases the severity of the pre-existing gastritis. This is especially true in gastrectomy for peptic ulcer since it is well-known that gastritis of varying degree is a usual accompaniment of peptic ulcer. The type of gastritis developing after gastric surgery may be one of any variety and does not conform to any pattern indigenous of postgastrectomy gastritis. The type of gastritis observed (mainly via gastroscopy) is the atrophic, hypertrophic, purulent and hemorrhagic varieties[1, 2]. Briefly the etiologic factors, either singularly or collectively, which may result in "stump gastritis" are:

1. Preoperative causes
   (a) Preexisting gastritis (present prior to surgery)

2. Postoperative causes

   (a) Physiological disturbances
      (1) Gastroesophageal sphincter dysfunction

   (b) Mechanical factors disturbing gastric physiology
      (1) Large stoma
      (2) Small stoma

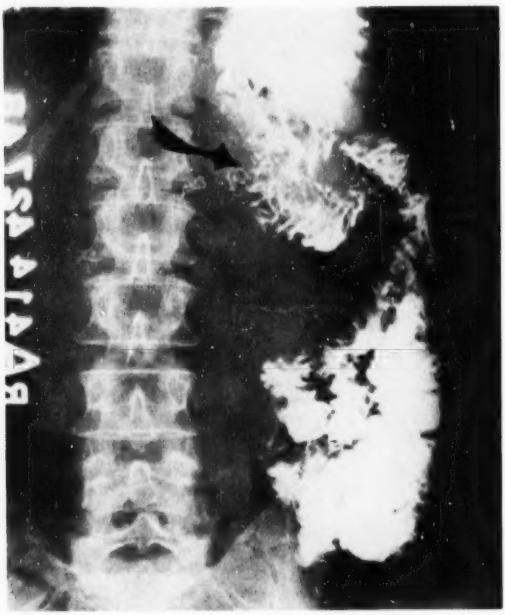

Fig. 4—Postgastrectomy hypertrophic gastritis associated with a jejunitis resulting in a gastrojejunitis.

      (3) High stoma
      (4) Low stoma
      (5) Improper jejunal loop

In those patients who have a preexisting generalized gastritis, it is to be anticipated that some disturbance in the residual gastric stump may be aggravated by surgery. The trauma of operation, the passage of gastric tubes, etc., cannot diminish the severity of the disease, but can only make it worse. Such patients usually have a preoperative high gastric acidity and should be candidates for a more radical gastric resection. They should be advised of the possibility that

certain symptoms may persist depending upon the preoperative picture and the findings at operation. This type of "stump gastritis" is the patient's inheritance concerning which the surgeon can do very little. In contradistinction to this preexisting gastritis is that type finding its origin in certain postoperative factors. It is in this group that the surgeon can be of real assistance and can use his talents to the utmost in order to prevent this disturbing complication.

Following the removal of a portion of the stomach, the surgeon attempts to reconstruct the nonresected segment of the stomach so that it may approach –as near as possible–the physiologic organ that was disturbed. Anatomic reconstruction is not as important as physiologic rehabilitation. The advocates of total gastrectomy have learned this lesson and realize that it is only half the battle to remove an entire stomach. The patient may become a physiologic invalid who has undergone major surgery without satisfying his body economy as a physiologic entity.

Any reconstructive procedure following partial gastrectomy aims at returning the stomach to its natural function as a reservoir for food and an organ of digestion. Reparative gastric surgery which fails in this regard may be a potent factor in the development of "stump gastritis". These surgical failures may be listed as the mechanical factors disturbing gastric physiology and center about the stoma and/or the jejunal loop.

Dysfunction of the stoma is one of the cardinal factors in the disturbance of postgastrectomy physiology which may instigate a "stump gastritis". Some gastroenterologists believe that a satisfactory physiologic stoma is one that demonstrates an automatic rhythmical pylorous-like activity regularly opening and closing with a stellar formation[3]. The stoma, which is too large, allows food to enter the jejunum immediately after eating. This does not allow for sufficient gastric digestion (softening and chymification) to occur. Under such conditions the "too large stoma" produces a dilation and an inflammation of the efferent jejunal loop (on occasion the efferent loop may become similarly involved). This inflammation does not remain only in the jejunum but "jumps" the anastomosis into the gastric stump. This dilatation and inflammation in the jejunum stimulates small bowel activity resulting in gaseous dyspepsia with excessive fermentation of starch and cellulose encouraged in the intestine[3].

The opposite situation in which a stoma is too small may also play a part in the development of "stump gastritis". A small stoma impairs the proper emptying of the remaining stomach. Regurgitation and vomiting occur during the postoperative hospital period. Although this condition may be temporary (due to edema) nevertheless the irritation resulting from the regurgitation and vomiting is sufficient to institute a gastritis. An obstructed stoma developing weeks or months after operation has a different background. For example an operation performed too soon on a dilated stomach may result in a small stoma. Following operation the dilated gastric remnant resumes its near normal size

with a corresponding decrease in the size of the stoma. The resultant stoma is now too small for proper physiologic emptying.

When a stoma is placed too high (or rises after a dilated stomach has diminished in size) it may be a factor assisting in the production of "stump gastritis". A high stoma may empty poorly and thus it would be similar to the impaired functioning of a stoma which was too small. The same criticism may be levelled against a stoma which is too low.

Following an antecolic anastomosis a disturbance in the emptying of the stomach and jejunum may occur if the afferent jejunal loop is too long. (Hence many surgeons advocate a short loop anastomosis.) In addition the accumulation of intestinal juices in the proximal loop interferes with a rapid neutralization of stomach acid. This delay and/or lack of acid neutralization predisposes to "stump gastritis". The regurgitation of intestinal juices into the stomach acts as a further irritant. This may produce vomiting which in turn further irritates the gastric mucosa and stimulates a gastritic reaction.

In addition to the factors mentioned above, there is a physiologic activity which is disturbed in subtotal gastrectomy when the pylorus is removed. This may or may not be a contributing factor to the development of "stump gastritis". The disturbed activity is the closing mechanism at the cardiac end of the stomach which produces the cardioesophageal closure after the passage of food from the esophagus into the stomach. This mechanism is associated with pyloric physiology in the normal stomach. The relationship between the pylorus and the cardia is an intercommunicating one which incarcerates the ingested food within the stomach until the initial phases of gastric digestion have occurred. After the proper digestive processes have occurred the stomach contents pass through the pylorus. Following gastrectomy with the removal of the pylorus, this mechanism may be abolished or inhibited. The result is that the cardioesophageal junction remains partially patent or functionally ineffective (often only temporary) with a subsequent regurgitation of gastric contents into the esophagus if and when an increasing quantity of food is ingested. This regurgitation is a source of irritation to the mucosa of the gastric stump.

Treatment

As in all pathologic conditions the preferred treatment is to prevent the disease whenever possible. In the prevention of "stump gastritis" those prophylactic procedures which can be utilized should be employed. For example in a patient with diffuse gastritis associated with a peptic ulcer, an adequate preoperative regimen should be followed which will diminish the severity of the gastritis or reduce it to a quiescent state, i.e., absence of bleeding, etc. Another prophylactic asset is to delay operation on a greatly dilated stomach until it has returned to near normal size. Where delay in operation cannot be allowed, then a stoma should be formed which is larger than usual and will

become adequate after the residual stomach returns to a non-dilated state. To prevent the occurrence of postgastrectomy gastritis, the surgeon at the time of operation should try to avoid those pitfalls which have been mentioned under the mechanical etiologic factors.

Finally when "stump gastritis" does occur, medical therapy is preferred rather than to subject the patient to further corrective surgery (aimed at shortening a jejunal loop or reconstructing a new stoma).

As to diet, the patient should follow a strict peptic ulcer diet until gastroscopic examination reveals sufficient improvement to allow a change. If x-ray studies demonstrated gastritis, the diet should be continued until improvement is noted via x-ray or gastroscopy. If achlorhydria and rapid emptying of the stomach or diarrhea are part of the symptom-complex, then frequent small feedings of bland food and small doses of hydrochloric acid after meals should be advised.

If nausea and vomiting are the major symptoms a readjustment and reevaluation of the patient's eating habits may prove advantageous. The patient should be advised to have small frequent feedings consisting only of bland foods. All food should be well masticated and "gulping" of food should be disadvised. A diet high in protein, cream and vegetable fats remains in the stomach longer than a diet abounding in starch. This protein-fat diet is better tolerated by such patients. At the same time the liquid component of the diet should be diminished. In those patients who have excessive intestinal flatulence, a preparation containing diastatic ferments may be prescribed after meals. When gastric acidity is high and diarrhea is present a powder containing belladonna, phenobarbital and bismuth may prove beneficial if given before meals. The use of roentgen therapy as advocated by some gastroenterologists has not found universal acceptance[3].

Prognosis

Proper and diligent treatment over a period of several months often corrects the postgastrectomy gastritis.

Summary

1. Attention is called to an infrequently discussed postgastrectomy complication.

2. This complication is postgastrectomy gastritis or "stump gastritis".

3. A presentation is made of the etiology and treatment of this pathologic entity.

4. Proper therapy (medical regimen) usually negates the necessity for corrective surgery.

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THE NEW GASTROSCOPIC TABLE

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If the time, effort and energy devoted to the development and use of the gastroscope had been less disappointing to the medical profession at large and the surgeon in particular, the procedure would have by now, gained wide-spread popularity in this country, because of the impetus given it in the Army and Veterans hospitals, during the latter part of the war and the early post-war period. In spite of the fact that the shortcomings of the gastroscope tends to discourage the beginner, frustrate the veteran and amuse the skeptic, the procedure is none the less of genuine value. Gastroscopy presents a vast potential and if the field is to be further developed and exploited to the utmost it must be the responsibility of the gastroscopist. We, who are trained in its use, are its only ardent supporters and, therefore, must devote as much thought as possible, first to further improve-

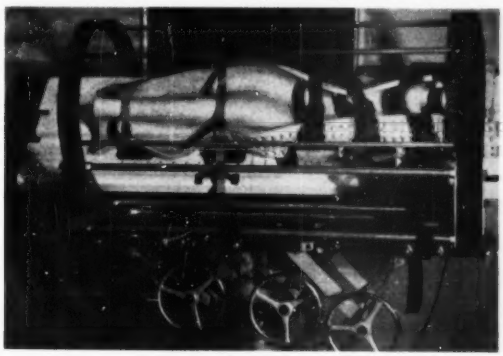

Fig. 1—The gastroscopic roto-table is seen fixed on the ordinary operating table. The rotating platform with the supporting straps and foam rubber pad is seen slightly tilted. This platform is removed, the patient fixed in place, and it is then reinserted through the right end of the machine. The patient is first rotated 360 degrees to familiarize himself with the procedure and to allay apprehension.

ment of the procedure and secondly to the presentation of the ever increasing value of gastroscopy, to the profession at large.

We have approached the problem from the point of view of the gastric surgeon convinced of the potential value of the procedure, yet dissatisfied with the end results. In spite of a stimulating apprenticeship under Dr. Rudolf Schindler and experience gained during the course of examining 248 patients, it is all too evident that improvements must be made if physicians are to seek gastroscopic consultation. Gradually there evolved the concept of examination during the course of constantly or intermittently changing position. The spit-like rotation principle was considered and recently the rotating table was devised.

This table upon which the patient may be placed, fixed in position, with the head and neck extended, can then be rotated clockwise or counter-clockwise through a range of 360 degrees. The table is constructed in such a manner that it may be clamped upon the ordinary operating table to attain motion in the vertical plane for lowering or raising the head or feet of the patient.

Although only seven patients have been gastroscoped using the "Gastroscopic Roto-table", it is quite evident these patients suffer no more discomfort during the examination than during gastroscopy when the routine left lateral position was used. There have been no accidents or untoward occurrences. It is our feeling that the visibility is considerably increased by the use of this maneuver because so many combinations of patient, as well as instrument, position relationship can be obtained.

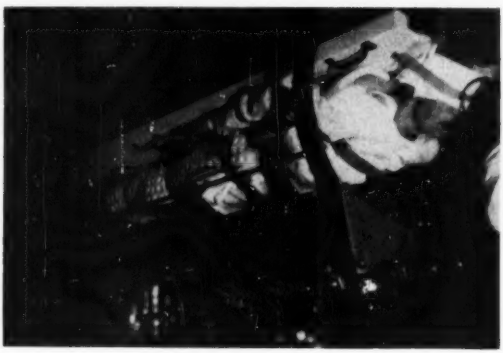

Fig. 2—The patient is fixed on the well-padded rotating platform which is brought to rest at the left lateral position after the initial trial rotation. The gastroscope is then introduced as usual, the examination begun and then rotation in either direction may be carried out during the observation.

Rotation of the patient can be arrested in any position desired while the head or feet can be raised or lowered at will. Using the new type table in combination with the omni-angle gastroscope, we have been able to see a good deal more of the prepyloric area and lesser curvature than ever before when using the old technic.

The gastroscopic table shown in these illustrations was designed and constructed by Dr. Karl Lang, Professor in the Engineering Department at the University of Kentucky. We have felt that by means of this principle several rather important features could be made available to the gastroscopist which might greatly increase his field of vision.

1. The position and relationship of the stomach to the gastroscope could be altered 360 degrees by completely rotating the patient about the instrument in contrast to simply rotating the instrument within the stomach.

2. The gravitational effect of this rotation of the patient would greatly alter the position of the stomach itself, as it swung between the fixed points of its extremities at the esophagus and duodenum.

3. By means of lowering the head of the table when examining the lower third of the stomach and reversing the procedure when examining the upper third of the stomach in combination with rotating the patient, far better views of the antrum, prepylorus and pylorus could be obtained on the one hand and of the fundus and cardia on the other.

Fig. 3—In this illustration the gastroscopic examination is in progress with the patient actually in the prone position having been rotated 180 degrees from the original supine position. Rotation carried on during the examination may be arrested or reversed at any point of practical interest or increased visibility simply by turning the two-way electric switch.

The photographs of the "Gastroscopic Roto-table", as it has been called, reveal the heavy construction and some of the rather awkward features of the table. The principle, however, is clearly illustrated. Many new alterations are already in the process of being incorporated in a lighter, more streamlined and efficient type of table which is now under construction.

This report of the new rotating Gastroscopic Table is being presented not because we feel this design is the mature and finished product, but simply to illustrate what appears to be a new, different and helpful addition to the technic of gastroscopy. The principle has not been found described in the literature. It is with sincere hope that others using this type of table may find the principle involved as useful and helpful in their hands as it appears to be in our own.

President's Message

Our Convention in Los Angeles is over, and it was an epochal event. To all the speakers, teachers, physicians, surgeons and others whose efforts made our convention a success, we extend our sincere thanks.

It would be impossible for me to adequately describe even the highlights of the convention in this brief message, so watch your REVIEW for the reports.

I do wish to announce, however, that our National Council unanimously passed a resolution to take steps to activate the American College of Gastroenterology.

For the past few years our National Council and our executive committee have been exploring and planning for the establishment of an American College of Gastroenterology. The College was incorporated under the laws of the State of Delaware in May 1952, and we have received our charter. It has also been registered in Louisiana, Michigan, California, New Jersey, and the District of Columbia.

The National Council has appointed a committee consisting of: Sigurd W. Johnsen, Chairman; Lynn A. Ferguson; James T. Nix; Arthur A. Kirchner; C. Wilmer Wirts and Frank J. Borelli to draw up the new Constitution and By-Laws.

When the Constitution and By-Laws have been accepted and approved, the remaining steps will be taken for an orderly transition from the National Gastroenterological Association to the American College of Gastroenterology.

Many problems remain to be solved but with the good will and cooperation which was manifested at Los Angeles this will be accomplished and we shall then embark on the next stage of expansion and cooperation of all who are interested in advancing the cause of gastroenterology.

Sigurd W. Johnsen

EDITORIAL

Hodgkin's Disease

About 35 per cent of patients with Hodgkin's disease exhibit gastrointestinal symptoms at some time during the course of the disease. In practically all such cases, however, these symptoms are not due to intrinsic lesions of the gastrointestinal tract.

At the present time no conclusions can be drawn as to whether Hodgkin's disease is a true neoplasm or granuloma. In this country the granuloma theory is more widely accepted. Parker found at autopsy a high percentage of associated tuberculosis, both healed and active. In the vast majority of cases, lymph node enlargement, usually cervical, is the first symptom to attract attention. Occasionally, because of bizarre manifestations, diagnosis may be perplexing, especially in the absence of nodular enlargement.

Two forms which are of interest to us are the abdominal or larval and the gastrointestinal type. They may occur without presenting enlargement of the superficial nodes. In the former, the disease involves only the abdominal nodes. Symptoms are vague and indefinite: remittant fever, diarrhea, ascites, diffuse abdominal pains, jaundice and hepatosplenomegaly. Longcope and McAlpin state that in the early stages cases have been mistaken for appendicitis, typhoid fever, tuberculosis or liver abscess; in the later stages for malignant growths.

In the gastrointestinal form, single large or multiple Hodgkin's tumors have been reported both in the stomach as well as in intestines. The sequelae of these cases, usually diagnosed at autopsy, were either massive hemorrhage or actual intestinal obstruction. Diagnosis depends upon micropathology. Hodgkin's disease, no matter where it may be present, has a similarity to its pathological pattern. The most satisfactory and conclusive method of differentiation is by histologic examination of an excised node. Classically the only cell which must be present in order to make the diagnosis is the Reed-Sternberg cell.

Prognosis is unfavorable, though surgical excision, irradiation and chemotherapy have their places in the treatment. X-ray and radiation are least effective in the gastroenterological form of the disease. Because mesenteric nodes sometimes form large masses capable of obstructing the common bile duct, surgery for its palliative effect may find more to recommend it in this type of disease. If undertaken it must be radical and should be followed by chemotherapy, i.e. nitrogen mustard.

Because the disease may produce such varied manifestations this disorder should be kept in mind, whenever such symptoms as relapsing fever, loss of weight, splenic or hepatic enlargement, together with an anemia present themselves for diagnosis.

Bernard Weiss, M.D.

ABSTRACTS FOR GASTROENTEROLOGISTS

GASTROINTESTINAL TRACT

OPTIMISM IN THE TREATMENT OF GASTROINTESTINAL CARCINOMA: H. M. Blegen. Postgrad. Med., 14:173-183, (Sept.), 1953.

The author presents eight case histories, the clinical pictures of which were those of advanced or hopeless cases of gastrointestinal carcinoma. All were operated upon and either cured or enjoyed long survival periods. Blegen emphasizes the difficulty in diagnosing or in developing a prognosis with such cases. Surgery revealed three with benign lesions; two with early cancerous involvement, and three who have enjoyed a long survival period. The essayist notes that it is difficult from a clinical evaluation to determine the extent or the curability of such lesions. Such factors as duration, size, and degree of emaciation are not infallible.

Dr. Blegen appeals for a prudent optimistic attitude and attempts at radical surgery even in the face of apparent hopelessness.

REGINALD B. WEILER

THE MANAGEMENT OF UPPER GASTOINTESTINAL HEMORRHAGE: T. A. Warthin, F. P. Ross, D. V. Baker, Jr. and E. Wissing. Ann. Int. Med., 39:241-253, (Aug.), 1953.

The mortality rate from bleeding peptic ulcer can be reduced from 5 to 2 per cent by a well trained staff. The indications in upper gastrointestinal hemorrhage are to treat the shock and restore an adequate circulating blood volume, to control the bleeding, to estimate the rate and manner of bleeding, to investigate the source of the bleeding, and to study the patient for evidence of significant complications.

This is a review of 5 years' experience at the West Roxbury Veterans Administration Hospital. There were 462 cases of bleeding from the upper gastrointestinal tract, of which 246 had massive hemorrhage. Treatment was instituted by a team composed of an internist, a surgeon and a radiologist. Prompt restoration of circulating blood volume by blood transfusion was considered essential in all instances. The authors advocate emergency gastrointestinal x-ray examination of all patients over 40 years of age as soon as they have been brought out of shock. The double balloon tube is used in the treatment of bleeding from esophageal varices.

Peptic ulcer accounted for 75 per cent of the upper gastrointestinal bleeding, while 25 per cent was due to esophageal varices, gastritis, polyps and carcinoma. They found that bleeding gastric ulcer constituted a graver and more serious hazard than bleeding from a duodenal ulcer. The prognosis was very poor in patients with esophageal varices, the mortality from massive hemorrhage in such cases being 80 per cent. Sixteen per cent of cirrhotics had coexisting peptic ulcers. Hematemesis remains a cardinal symptoms of major hemorrhage.

Thirty-two patients were operated upon an emergency or urgent basis, only one death being recorded. If no source of bleeding is found and the hemorrhage is over 3 liters of blood a day for more than 48 hours, the patient should be explored to determine the highest level of blood within the gastrointestinal tract and subtotal gastric resection done if necessary. They stress

the necessity for early operation in cases of bleeding gastric and postbulbar duodenal ulcers, which are especially prone to bleed uncontrollably. Other systemic complications, such as diabetes and heart disease, increase the hazard of ulcer bleeding and point toward early surgical intervention.

ARNOLD STANTON

STOMACH

PRIMARY BENIGN PEPTIC ULCERS OF GREATER CURVATURE OF STOMACH: Lester Baker, and Fred A. Gattas. A.M.A. Arch. Int. Med. 92:321, (Sept.), 1953.

Four benign peptic ulcers of the greater curvature of the stomach proven by histological examination of surgical or autopsy specimens are added to the 33 well documented cases previously described in the literature. Overall incidence is estimated to be 1 per cent of all gastric ulcers. The majority of cases are either not properly diagnosed or documented. Clinical symptomatology of such lesions may be characteristic of peptic ulcer or may be nonspecific. A correct x-ray diagnosis can usually be made with the use of mucosal pattern and pressure spot technic. An ulcerating lesion with a small edge of malignancy is still a difficult diagnostic problem, even for the pathologist. Gastric acidity in benign ulcer may be normal or low, free hydrochloric acid may be absent. Repeated gastroscopy was unable to delineate the ulcer crater in two cases because of overhanging mucosa folds. Differential diagnosis must consider aberrant pancreas, ulcerated Schwannoma, congenital and acquired syphilis, tuberculosis, mucosal pockets of hypertrophic gastritis, ulcerative antrum gastritis, gastric and duodenal diverticula and malignancies.

H. B. EISENSTADT

RADICAL GASTRECTOMY FOR BENIGN GASTRIC ULCER: A. M. Boyden. Surg. Gynec. & Obst., pp. 151-158, (Aug.), 1953.

A review of the records of all patients operated on at the Portland Clinic for gastric ulcer and gastric carcinoma during a six year period from 1946-1952, confirmed the fact that in a high percentage of cases benign and malignant ulcers are indistinguishable either preoperatively or at operation. This results in complete inadequate operation in those patients proving to have malignant lesions. To circumvent this possibility, the authors advocate radical subtotal gastrectomy for all gastric ulcers. There has been no increase in operative mortality resulting from such extension from simple ulcer resections. The authors in this article re-emphasize the use of radical gastrectomy, total and subtotal in the treatment for benign gastric ulcer.

J. R. VAN DYNE

DUODENUM

DEVELOPMENT OF NEW SYMPTOMS FOLLOWING MEDICAL AND SURGICAL TREATMENT FOR DUODENAL ULCER: James S. Browning, and John H. Houseworth. Psychosomatic Medicine 15:328-336, (July-August), 1953.

It has been postulated and demonstrated by psychoanalysts that organic symptoms, in which psychopathology is an important factor, are perverted expressions of the intrapsychic conflicts; and not isolated manifestations of pathology or pathophysiology, primary in themselves.

The authors set out to investigate the hypothesis that elimination of duodenal ulcer symptomatology by physical means might result in the development of new symptoms. In the experimental group there were thirty patients whose duodenal ulcers were treated by gastrectomy, which resulted in 57 per cent becoming symptom-free. The control group consisted of thirty patients with doudenal ulcers who were treated medically, and in whom complete symptom-remission did not occur. Follow-up investigation revealed that the surgically treated patients had a significant decrease in ulcer symptoms, but that this was *compensated*

for by a significant parallel increase in other psychosomatic and psychoneurotic symptoms. The medically treated group, in which no significant decrease of incidence or severity occurred, revealed *no such redistribution of symptoms.*

The authors conclude that psychoanalytical findings are substantiated and that their research project sustained the hypothesis that successful removal of duodenal ulcer symptoms, without resolution of the associated psychopathogenic conflicts, may result in the development of new symptoms.

The conclusions reached are that the medically treated group, who still have the original ulcer symptoms, have not tended to develop new symptoms, while the gastrectomy group, who were largely relieved of their original symptoms, have developed an increasing number of new symptoms.

REGINALD B. WEILER

FAMILIAL HYPERTROPHIC PYLORIC STENOSIS: T. Fenwick. Brit. M. J., 2:12 (July 4), 1953.

A family with hypertrophic pyloric stenosis is reported. Five members, all males, were affected, the trait was transmitted through males as well as females. A 39 year old member of the family had spells of epigastric pain and tenderness occurring from a few minutes to up to one hour after meals. Pain persisted for 20-60 minutes and was relieved by vomiting. Attacks occurred for over 10 years. X-ray showed an elongation and narrowing of the pyloric canal with concave indentation of the duodenal bulb. Patient was treated by Billroth I partial gastrectomy, mainly because the correct preoperative diagnosis was not made. Differentiation of benign pyloric stenosis from ulcer, cancer and gastritis might be difficult even during laparotomy. Ramstedt's operation is the standard procedure for children but has not proven too successful in adults where Billroth I pylorectomy or even Billroth I partial gastrectomy gives better long-term results.

H. B. EISENSTADT

INTESTINES

NEUROPSYCHOLOGICAL SYMPTOMS IN COLITIS: R. Catlan. Gaz. Med. France, 59:1193-1197, 1952.

Syndromes frequently observed by Catlan include diffuse headache or cranial paraesthesias, migraine, sensory disturbances such as hemianopsia, visual blurring; vertigo, lipothymia, syncope which usually was observed during remission of the intestinal symptom and something which the author calls "colitic epilepsy". In diagnosing such cases, the possibility of projected anxiety and "psychopathic preoccupations" reflected onto the digestive tract must be explored. He maintains that differential diagnoses is not difficult, because "proper therapy will resolve the symptoms". All possible etiological factors such as parasitic infections should be considered and receive adequate treatment. He also recommends measures directed toward restoration of autonomic imbalances.

REGINALD B. WEILER

PSYCHIATRIC FINDINGS IN CROHN'S DISEASE: R. W. Crocket. Lancet 1:946-949, 1952.

A brief review of the literature is followed by sixteen abbreviated case histories. Employing the method of a single psychiatric interview, the author concludes that there is no "substantial evidence" that emotional stress plays a major etiological role in regional ileitis, "but that it does in the formation of symptoms" in some patients. Either a state of dependency or of immaturity was noted.

The reviewer feels that a method employing but a single interview is totally inadequate to arrive at the conclusions here elucidated. Unconscious material and character resistances can scarcely be evaluated by such superficial means.

REGINALD B. WEILER

MULTIPLE ORGAN RESECTION FOR ADVANCED CARCINOMA OF THE COLON AND RECTUM: J. Van Prohaska, M. C. Govistis, and M. Wasick. Surg. Gynec. & Obst., pp. 177-182, (Aug.), 1953.

The authors conclude that extension of carcinoma of the colon and rectum into another organ or structure is not necessarily a contraindication to curative or palliative surgery. Resection of the primary lesions in continuity with the involved adjacent organ or structure increased the rate of resectability by 9 per cent. It is concluded that exploratory dissections of neoplastic masses without compromising blood supply might convert seemingly hopeless cases into resectable ones.

J. R. Van Dyne

PSYCHOSOMATIC PROCTOLOGY: A. J. Cantor. Am. J. Psychother., 6:449-466, 1952.

In a high percentage of colonic complaints, no organic pathology is found. These are probably caused by emotional conflicts. In others, superimposed on tissue change, is a psychogenic factor. The author lists the following as common psychosomatic colonic diseases: Mucous colitis, ulcerative colitis, many cases of constipation or diarrhea, pruritus ani, colonic motor neuroses, nontraumatic coccygodynia, proctalgia fugax, some cases of rectal traumata, and foreign bodies in the rectum.

Cantor claims to be able to diagnose emotional conflicts by having the patient complete a "conflict check chart". He then treats his patients by a sort of abreaction and desensitization followed by reeducation. He claims "cures" in from 3 to 8 hours of psychotherapy.

No doubt, the symptoms may be relieved by this program especially because of Cantor's prestige and interest. But, there is considerable difference between relief of symptoms and cure. I wonder how many of Cantor's patients relapse and how many develop other organic or emotional complexes to replace the expression for which the colonic syndrome was the outlet.

Reginald B. Weiler

PRURITUS ANI: Ida Macalpine. Psychosomatic Med., 15:499-508, (Sept.-Oct.), 1953.

Pruritus ani is characterized by intense itching, refractoriness and preponderance in males. However, it is always associated with bizarre gastrointestinal symptoms and sexual disorders. Concomitant therewith, depressive and paranoid trends are common. Therefore, the pruritus is the dramatic symptom characteristic of a syndrome. Its origin lies in infantile unconscious fantasies concerned with procreation centering around the anal psychosexual period. The somatic symptoms represent a reaction to these archaic fantasies which are incompatible with reality. Thus, the symptoms are defenses against a psychotic breakdown. Psychotherapy is capable of resolving the syndrome. The author feels that this disorder is allied to hypochondriasis.

Reginald B. Weiler

THE RELATIONSHIP OF CHRONIC ULCERATIVE COLITIS AND CIRRHOSIS: F. W. Hoffbauer, J. S. McCartney, C. Dennis, and K. Karlson. Ann. Int. Med., 39:267-284, (Aug.), 1953.

The authors reviewed 287 patients at the University of Minnesota Hospitals between 1934-1952 and found 12 cases with the development of cirrhosis following a period of ulcerative colitis. Four of the patients had postnecrotic cirrhosis, which progressed to a relentlessly fatal termination. Patients with chronic ulcerative colitis have many opportunities to develop a homologous serum hepatitis, and this may well be the factor which produces the cirrhosis, or infectious hepatitis may occur with resultant cirrhosis.

In five patients the diagnosis of cirrhosis was established on the basis of physical, laboratory and biopsy findings. In seven patients autopsy findings were available, although the terminal clinical manifestations were typically those of advanced cirrhosis, such as bleeding from esophageal varices and hepatic coma.

The authors conclude that the relationship of ulcerative colitis to the development of cirrhosis is obscure, although the coincidental occurrence of the two diseases may be greater than is generally appreciated.

Arnold Stanton

CUTANEOUS METASTASIS OF ADENOCARCINOMA OF THE RECTUM AND SIGMOID: Ray H. Burnikel, and Robert T. McCarty. Postgrad. Med., 14:191-197, (Sept.), 1953.

Malignant tumors are characterized by their ability to form metastases. Frequently only lymphatic transmission is considered as the sole method of spread and the possibility of hemogenesis of the secondary involvement overlooked. Adenocarcinomas of the rectum and sigmoid mestastasize rather freely and often the site is located far from the original lesion. The authors present two cases of cutaneous metastatic involvement originating in cancers of the rectum and sigmoid colon. They present a thorough discussion of the possible routes of dissemination.

REGINALD B. WEILER

REOPERATED CONGENITAL MEGACOLON: R. B. Turnbull, and L. J. McCormack. Cleveland Clin. Quart. 20:339-345, (Apr.), 1953.

A case of congenital megacolon or Hirschsprung's disease is reported in which reoperation was performed because of initial failure to remove the aganglionic upper rectal segment. Usually, simple resection of the dilated, hypertrophic colonic segment alone may restore the patient's bowel function to normal for a number of years. However, failure to remove the aganglionic segment may eventually result in recurrent megacolon with physiologic obstruction, necessitating reoperation.

ARNOLD L. BERGER

ALLERGY

THE POSSIBILITIES OF A ROENTGENOLOGICAL DIAGNOSIS IN ALLERGIC DIGESTIVE DISORDERS: G. F. Leroux, and L. Ruyters. Acta Gastro-enter. Belg., 16:4, (April), 1953.

The authors review the lesion which could be detected by roentgenology. They have considered successively the radiological aspects involved by motility, secretory and edematous modifications in the digestive tract itself and in the gallbladder.

The authors have come to the conclusion that these aspects are not specific, and propose defining the criteria to be applied during the experimental releasing of the anaphylactic crisis.

FRANZ J. LUST

ENDOSCOPY IN DIGESTIVE ALLERGY: N. Buyssens. Acta Gastro-enter. Belg., 16:167, (April), 1953.

In the esophagus, the existence of an edema which closely resembles angioneurotic edema has been noticed. Good therapeutic results with antihistaminic drugs are mentioned. In the stomach, two types of lesions are seen: atrophic gastritis with congestion, hemorrhages and sometimes erosions in the more recent cases or in acute exacerbations of chronic cases. Experiences on dogs confirm the findings. Attention is drawn to the localization of the lesions at the antrum and the angulus. The existence of a pure functional allergy without mucosal lesions but with strong peristalsis is stressed. Except for ulcerative colitis, endoscopic examination of the rectum in allergy has been negative.

FRANZ J. LUST

PATHOGENESIS OF ALLERGY: Jean Lederer, Marie-Henriette Spyckerelle-Gelders. Acta Gastro-enter. Belg., 16:4, (April), 1953.

The meaning of allergy is discussed. The antigens are usually proteins of a high molecular weight, but some rather simple bodies may act as an antigen (Haptens).

The antibodies are gamma globulins. They are formed either by the reticulo-endothelial system or by the lymphocytes or plasmocytes. It has been made possible to show the occurrence of antibodies by injection of the antigens in the skin, by passive sensitiva-

tion or by the fixation of the antigen on red blood cells.

It has been established that the antibodies may circulate in the blood or that they may be located in the tissue cells. In the first case after the administration of the antigen, the shock is almost instantaneous, in the other case, the reaction is delayed.

The symptoms of allergy are determined by the combination of the antigen with the specific antibodies. As a rule, histamine is then set free. The antigens may enter the body through the alimentary tract or reach the digestive system through the systemic circulation. The relations between allergy and the adrenal cortex are outlined.

The allergic man and the adrenalectomized animal behave alike in some way, but cortisone and the antihistaminic drugs differ almost completely in their pharmacodynamic peculiarities. Cortisone acts only on tissular allergy, while antihistaminic drugs alleviate the reactions of allergic shock.

FRANZ J. LUST

THERAPY IN DIGESTIVE ALLERGY: R. Le Cluyse. Acta Gastro-enter. Belg., 16:195, (April), 1953.

The author gives the principles in therapy:

1. Change of the ground on which allergy develops: for this purpose one prescribes daily a series of empirical therapeutics (hyposulfites, calcium, milk parenterally, autochemotherapy, etc.).
2. Therapy trying to avoid the conflict antigen-antibody.
   a. Investigations to find the antigen, and suppress it.
   b. Pseudodesensibilitation, specific if possible, or aspecific. (desensibilisation by mouth, or parenteral, peptone, vaccine).
   c. An attempt be made to avoid the formation of antibodies (nitrogen mustard, ACTH?).
3. If the antigen-antibody conflict happens, minimisation of the effects of the allergic reaction by means of antihistaminic drugs, hormontherapy by ACTH or cortisone.

FRANZ J. LUST

STUDY OF THE ANATOMICAL AND EXPERIMENTAL ALLERGIC REACTIONS: J. Firket, V. Conrad, and J. Lecomte. Acta Gastro-enter., Belg., 16:235-281, (April), 1953.

Acute digestive phenomena (hyperperistaltism, mucus hypersecretion congestion of the mucous membrane with an edema sometimes directly appreciable) are often accompanying the anaphylactic shock in man.

The same gastrointestinal phenomena ascertain the course of the affections whose allergic nature is revealed by their well defined starting agent and accompanying symptoms such as rheumatoid purpura. The reality of a response of the digestive tract to the allergic aggression is thus so established. We were only able to isolate for sure, in the course of our analysis of the microscopic criteria of tissue reactions, presumptive signs in favor of the allergic origin of such or such syndrome, and only when considering these criteria as a whole.

The lack of precision of a functional symptomatology of banal appearance and the absence of specificity of the studied lesions compel the physician to restrict his statement of the allergic nature of any gastrointestinal affection to the case when he is in possession of a particularly convincing collection of clinical and humoral arguments. They must comprise positive familial and personal antecedents, the reproduction of the digestive disorders by the introduction of the incriminated substance, their regular vanishing by its eviction, and, at last, the detection of antibodies either circulating or tissular, by tests clinically appropriate to the phenomenon under study.

However rigorous those requirements may appear, they are essential to make possible a proper reply to the question: "allergy or not". There is too much similitude, indeed, between those tissular and functional reactions that are obtained during specific allergic manifestations and those of the aspecific strain provoked by violent stress. Too many pharmacodynamic actions are devolved to substances known as antihistaminic or antiallergic for an argument to be possibly constructed on their therapeutic power in favor of a given pathogeny.

In addition to the main acute anaphylactic syndromes whose digestive reactions are nothing but symptoms among an obvious

entirety (anaphylactic shock, edema of Quincke, generalized urticaria) or the main reaction to the parenteral introduction of an antigen duly identified by specific lesions (gastric or enteric Arthus), few syndromes will resist criticism, with perhaps the exception of Schonlein-Henoch's anaphylactoid purpura.

Local digestive reactions will be still more difficult to diagnosis etiologically. Of course, when they meet the above criteria, the gastric ulcus, intestinal infarction, gangrenous cholecystitis, regional ileitis, necrosing appendicitis, may reveal an allergic origin. But, under the present state of our knowledge in the matter, we are unable to conclude from the particular to the general and to affirm, for each of them, a pathogenic unity that does not seem to exist at all.

FRANZ J. LUST

SOME CLINICAL ASPECTS OF DIGESTIVE ALLERGY: J. Massion, J. Godart, P. Leonard, R. Van Leberghe, and J. Jamar. Acta Gastro-enter. Belg., 16:289-345, (April), 1953.

In contrast to the acute manifestations of digestive allergy, relatively easy to recognize, the digestive troubles of chronic allergy are rather difficult to diagnose. The diagnosis of chronic digestive allergy is of a clinical order, for the clinician has to evaluate the skin tests along with the anamnesis, the essential facts of which are studied, the skin tests and the diet of provoked elimination force the conviction. Skin tests are positive in a limited number of cases only.

In the mouth, the vesicles are a frequent sign of allergy. The same holds true for stomatitis of a contact reaction. In the esophagus, an unexplained dysphagia compels one to look for allergy. As for the stomach and duodenum, the insufficiency of hydrochloric acid plays a favoring role. The symptoms in the chronic forms consist essentially of, either periodic vomiting or pylorospasm, or a burning sensation. Pains are seldom found. The gastroduodenal ulcer does not seem to be an allergic condition except in certain cases where allergy contributes to its appearance. Gastroscopy is a valuable help. As for the duodenal bulb, radiology with the allergen has been found useful. Liver and bile are studied separately. On the allergic bile cyst of the animal, contractile and inflammatory reactions are noted, common to allergic reactions. In clinical practice, the cystic crisis takes on a peculiar form: the cystic duct and the sphincter of Oddi may react in their turn. It is difficult to codify the radiology in the digestive allergy. In some sequelae of cholecystectomy, a microbial factor might intervene through an allergic mechanism. The liver is necessary to the occurrence of an allergic shock. The allergic liver crisis and the edematous hepatitis of intolerance are classified with the allergic reactions in man. The biology of the liver allergy does not show any insufficiency within the classical meaning of this term. Perhaps signs of functional hyperactivity should be sought. Normal or exaggerated functions of the liver also seem in the experiment to be conditions necessary for the production of liver allergy.

As for the intestine, purpura fulminans and some cases belonging to the surgical pathology (mesenteric infarcts) are of an allergic origin. The acute allergic enterocolitis will be easily recognized. As for the chronic disorders, their very common symptomatology (ballooning, spasms, hypersecretion, rarely bleeding) makes them both more frequent and less easy to demonstrate. Radiology with the allergen is a good sign of allergy. In the colon, the intervention of the microbic flora complicates the problem. In the early dumping syndrome in patients after gastrectomy, allergy seems to be part of the problem, as in small intestinal specimens of such cases, signs of an allergic disorder were found.

FRANZ J. LUST

PSYCHOSOMATIC MEDICINE

A THEORY OF THE ORIGIN OF GASTRIC AND INTESTINAL ULCERS: A. Garma. Psyche, 6:293-303, 1952.

Ulcer patients force themselves into activity, independence, and strive for material recognition. But deeper unconscious drives are in the direction of passivity and dependence. These unconscious urges give rise to the ulcer pathology because of the conflicts between the conscious and unconsious complexes. A similar tension exists in the libidi-

nal conflicts which produce difficulties between independence and dependence upon a sexual object; and the resulting frustrations. The author formulates an involved theory concerning a mother-ideal which is opposed to the oral receptive dependency desires which find expression through digestive activity.

REGINALD B. WEILER

THE PERSONALITY OF DYSPEPTICS, WITH SPECIAL REFERENCE TO GASTRIC AND DUODENAL ULCER: Max Hamilton. Brit. J. Med. Psych., 23:182-198, 1950.

The author has made a comparative study of four groups of patients, each group consisting of fifty patients. The groups were divided: (1) Duodenal Ulcer; (2) Gastric Ulcer; (3) Nonulcerous Dyspepsia; (4) Controls. All were male and a complete personal and social history was made in each one. After careful statistical study the conclusions reached include: The group of nonulcerous dyspeptics is characterized by anxiety, guilt, dependence and inability to adequately handle difficulties. The author feels that this array of symptoms are similar to those of an anxiety neurosis, and therefore considers such cases essentially anxiety neuroses.

The duodenal ulcer group showed less of these characteristics than the dyspeptic group and the gastric group less than the duodenal ulcer group. The controls showed least of all. The gastric ulcer group was differentiated from the duodenal ulcer group by a greater dependency, perfectionism, and an inability to work intensively. Both of the ulcer groups were more independent, but less able to work hard than the two non-ulcer groups.

REGINALD B. WEILER

PSYCHIATRIC DIFFICULTIES ASSOCIATED WITH EATING: C. H. Hardin Branch, and David E. Reiser. Rocky Mountain M. J., 50:728-733, (Sept.), 1953.

This article is an excellent exposition of neurotic symptoms associated with food. It is accompanied by seventeen clever drawings, illustrating the text.

In patients exhibiting food symptoms, but whose neuroses are not too severe, much can be learned through investigation of the attitudes toward food, obesity and digestion. Symptoms involving ingestion and assimilation may serve as defenses against problems of living, or in order to bind anxiety. Such symptoms afflict women more often than men. They are associated with interpersonal difficulties, as well as sexual immaturity.

Peptic ulcerations, ulcerative colitis, capricious appetites, anorexia, under- or overweight, and food idiosyncrasies are all included among neurotic food conditions. Also included are patients who cannot stay on therapeutic diets. Such symptoms are observed in depressions, obsessive-compulsion, schizophrenia, and the hysterias.

There is an excellent discussion of the genesis of food fantasies, enhanced by the humorous method of presentation.

A general plan of psychotherapy is suggested.

REGINALD B. WEILER

PSYCHOSOMATIC CONDITIONS: A. Poslavsky. Geneesk. bl. (Utrecht), 45:215-239, 1952.

The author discusses two cases, one of peptic ulcer, the other of asthma; based upon which he discusses psychosomatic conditions in general. He is interested in trying to discover distinguishing features characteristic of psychosomatic cases. He concludes, based upon the cases presented, that such patients besides exhibiting "specific" unconscious patterns, drives and inhibitions; also had unique difficulty in establishing interpersonal relationships which is characterized in the therapeutic transference. Also, there is a limitation in their ability to express affects. The author concludes that a combination of object relationship difficulties, specific personality profiles with predeliction to peculiar somatic pathology characterizes these disorders.

REGINALD B. WEILER

A CASE OF ALTERNATING EMACIATION AND OBESITY OF PSYCHOSOMATIC ORIGIN: J. L. M. Sinnige. Evolut. Psychiat., 2:327-337, 1952.

The case described is one in which there was alternating emaciation and anorexia with obesity. The author concludes that an identical psychogenesis is responsible for both phases. This is fundamentally a fixation of the psychosexual development at the oral stage. Obesity and emaciation are merely reflections of the ego defenses against oral sadistic (cannabalistic) urges. These defenses consist of oral activity (aggression) in the obese symptom with the reactive defense of anorexia, which gives rise to emaciation, and which consists of an inhibition and successful repression of the oral cannabilistic demand with the reaction-formation (over-compensation) of inhibiting any oral intake.

REGINALD B. WEILER

A PSYCHOLOGICAL STUDY OF PEPTIC ULCER PATIENTS: D. P. Marquis, E. R. Sinnett and W. D. Winter. J. Clin. Psychol., 8:266-272, 1952.

Sixteen male patients with active peptic ulcers were subjected to a battery of psychological tests. These divided the group into two sections: "primary" and "reactive" types. Both groups exhibited marked oral fixation; sexual maladjustments, secondary to strong dependency needs; feelings of inferiority; and anxiety reactivity. The "primary" type recognized the dependency and accepted it with active attempts at seeking gratification; while the "reactive" type denies and represses the dependency drive.

REGINALD B. WEILER

BEHAVIOR OF THE STOMACH DURING PSYCHOANALYTICAL THERAPY: S. G. Margolin. Psyche, 6:443-459, 1952.

In a 22-year-old female patient with a gastric fistula, a study was made of gastric motility, blood supply, secretory activity, HCl concentration and pepsin secretion under varying stresses during psychoanalytical treatment. The author found that characteristic physical responses were not correlated to any specific personality profile. He feels they are due to the various emotional complexes resulting from changeable interactivity between the defenses, the drives, and the transference relationship. These several reactions recur in specific patterns, and thus are predictable. This patient's functions were simultaneously enhanced when repressed drives threaten to break through. When the defensive reaction-formation ensued, the various functions were all inhibited. When a new level of relative homeostasis developed, the individual functions became dissociated. It was found that a predictable relationship exists between these psychophysiological observations and psychoanalytical findings. Physiological states could be reproduced by utilizing psychoanalytical technics.

REGINALD B. WEILER

EMOTIONS AND HYDROCHLORIC ACID SECRETION DURING PSYCHOANALYTIC HOURS: George F. Mahl, and Richard Karpe. Psychosomatic Medicine, 15:312-326, (July-Aug.), 1953.

These two authors, through the psychological study of two cases, try to formulate one theory and refute a second. The investigation deals with the relationship of relative intensities of emotions to the degrees of gastric hydrochloric acid production. They conclude that hydrochloric acid secretions increase with anxiety associated with sexual hostility and passive-dependent wishes. They insist that no hydrochloric acid increase occurs because of such needs but rather because of anxiety.

The case histories demonstrate that both patients were torn by conflicts between dependency needs and mature genitality. Whenever the gastric acid values were depressed the material produced portrayed oral-dependent regression. In the sessions at which the gastric acidity was high, the patients revealed a reactivity against dependency on the analyst. The essential factor in producing alterations lies in the psychic defenses.

REGINALD B. WEILER

GASTRIC ACIDITY AND NORMALLY PRODUCED ANXIETY: Melvin H. Heller, Jacob Levine and Theodore P. Sohler. Psychosomatic Med., 15:509-512, (Sept.-Oct.), 1953.

Ten patients were each given two gastric intubations on two successive days. Each patient manifested anxiety because of the need of the second investigation. Free and total gastric acid secretion showed, in every case, levels which were significantly elevated on the second day; and these elevated values were maintained throughout the entire day. The authors attribute the raised values to anxieties engendered by the situation. No significance was found in the relative elevations of acid levels between patients with and without upper gastrointestinal symptoms.

REGINALD B. WEILER

PATHOLOGY AND LABORATORY RESEARCH

THE BORIC ACID PROBLEM: Clement E. Brooke. G. P., 7:43, (June), 1953.

Boric acid poisoning occurs mostly in small children treated with boric acid preparations for diaper rash, but may be found in adults receiving such treatment for extensive burns or skin diseases. The slow rate of excretion permits the substance to accumulate in the body until lethal or near lethal amounts are present. Symptoms develop gradually and consist of anorexia, nausea, vomiting, diarrhea and dysentery. The characteristic intense erythema of skin and mucous membranes and the central nervous system irritation seen in children is frequently absent in adults. The possibility of boric acid poisoning has to be considered in all persons with extensive skin lesions or burns showing gastrointestinal symptomatology. As the antiseptic value of boric acid is slight its use in medicine should be abandoned.

H. B. EISENSTADT

THE METABOLIC EFFECTS OF ACTH AND CORTISONE IN NONTROPICAL SPRUE: Joseph E. Giansiracusa, T. L. Althausen, Grant W. Liddle and Phillip Perloff. Am. J. Med. 15:415, (Sept.), 1953.

Four patients with nontropical sprue were subjected to clinical and metabolic balance studies before and after treatment with ACTH and Cortisone. A favorable clinical response of all patients was observed. Fecal excretion of fat was unchanged and sometimes increased during treatment with these hormones. The flat Vitamin A tolerance curves characteristic of sprue were markedly raised during administration of ACTH. These paradoxic observations were explained by a dual effect of the hormone producing increased intestinal absorption of ingested fats as well as increased enteric excretion of endogenous fat. No significant changes of fecal nitrogen, phosphorus and calcium were observed.

H. B. EISENSTADT

BOOK REVIEWS FOR GASTROENTEROLOGISTS

1952 YEAR BOOK OF ENDOCRINOLOGY: Edited by Gilbert S. Gordan, M.D. 400 pages, illustrated. The Year Book Publishers, Inc., Chicago, Ill., 1953. Price $5.50.

Endocrinology as it appears in this year book makes easy reading and discusses the more recent developments in this field. A very interesting and timely discussion regarding basal metabolism and its evaluation appears on page 6 in the introduction. This should be carefully read by the general practitioner, so that he may evaluate the true cause of increased and decreased B.M.R. readings. The newer diagnostic procedures far supplant the old method as utilized for determining the thyroid function.

Other interesting features discussed are the adrenals, cortisone and allied compounds, hematologic disorders, etc. Treatment of neoplastic diseases with endocrines and other miscellaneous diseases are covered.

RESPIRATORY DISEASES AND ALLERGY: Josef S. Smul, M.D. 80 pages. Medical Library Co., New York, N. Y., 1953. Price $2.75.

This new handbook on Respiratory Diseases and Allergy is a valuable addition to the physician's library. It is well written, concise and practical in presenting the author's views on a controversial subject.

MEDICAL PROGRESS—A REVIEW OF MEDICAL ADVANCES DURING 1952: Morris Fishbein, M.D. 300 pages. The Blakiston Co., New York, N. Y., 1953. Price $16.00.

Under the able editorship of Fishbein and the array of prominent contributors, Medical Progress—1952, should prove to be valuable in briefing the physician of the progress made in 1952. In glancing over the contents, one will find that "medicine" both internal and external, has been covered. The summary notes by Fishbein complete the test.

It is highly recommended to the busy physician for after-hours reading.

DISEASES OF THE DIGESTIVE SYSTEM: Edited by Sidney A. Portis, M.D. 1119 pages. Third edition, thoroughly revised with 269 engravings and 5 color plates. Lea & Febiger, Philadelphia, Pa., 1953. Price $20.00.

If the reviewer had his choice, he would stick to Portis' book on "Diseases of the Digestive System". In this magnificent volume, the general practitioner as well as the gastroenterologist will find clear and concise explanations of the wheres and whys in diseases of the alimentary tract.

The large list of clinicians contributing to this volume makes it a living encyclopedia. There are 54 chapters, each one written by a specialist.

A very interesting chapter, page 253, deals with hyperinsulinism and fatigue and its diagnosis and treatment. The use of atropine in small doses, 1/300 gr. to 1/500 gr. is prescribed by the reviewer, who noted similar effects upon the patient's well being as described by Portis. Reduction of the dose or withdrawing it, caused low blood sugar and the return of fatigue. Further suggestion in restriction of sugar and carbohydrates, especially the readily soluble type, resulted in improving the fatigue syndrome.

The use of antibiotics and other therapy is ably discussed.

Clinicians and physicians teaching undergraduate and graduate gastroenterology will find this volume indispensable and should recommend it to the students.

The editor as well as the publishers are to be commended for bringing out this excellent text.

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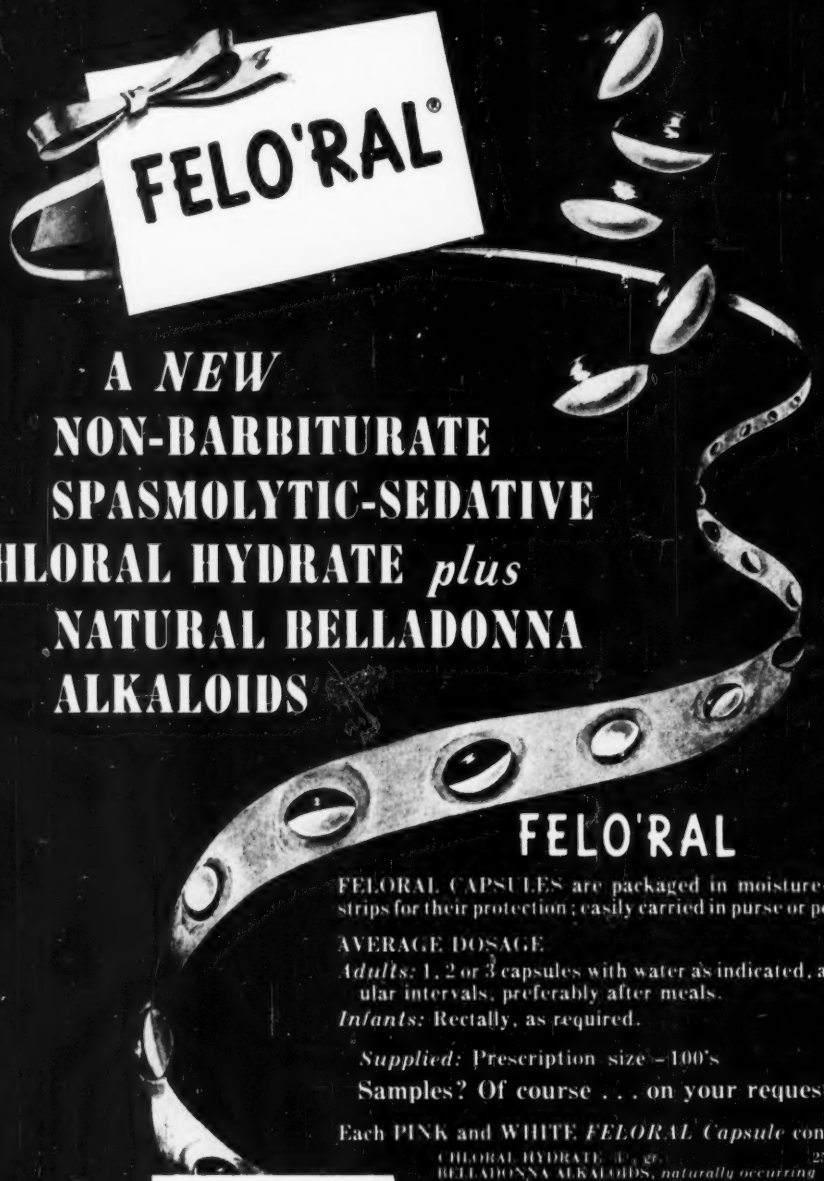

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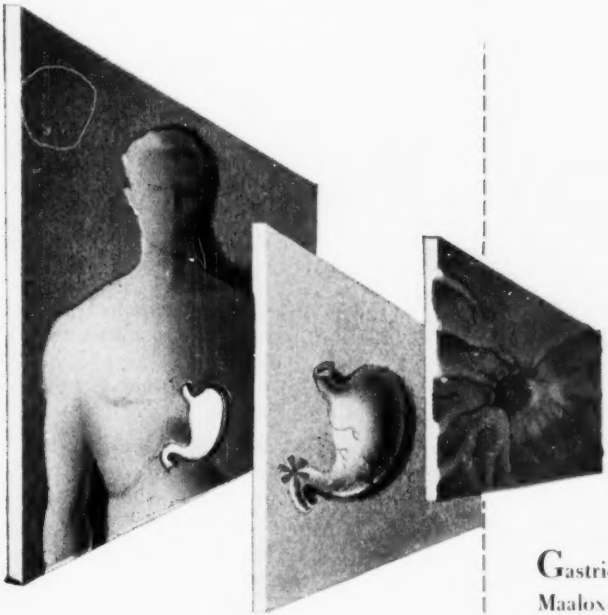

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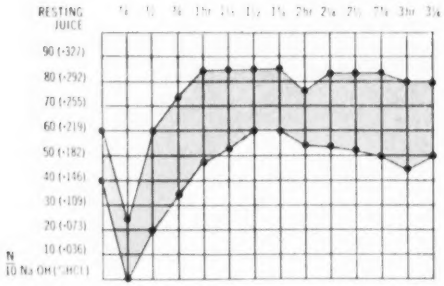
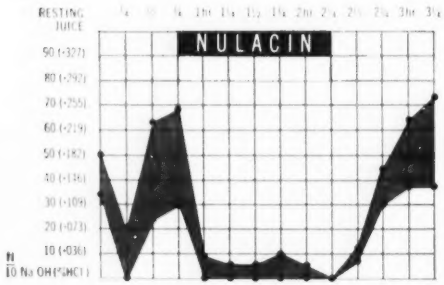


GASTRIC ANALYSIS. Superimposed gruel fractional test-meal curves of five patients with peptic ulcer.



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1. Douthwaite, A. H., and Shaw, A. B.: The Control of Gastric Acidity, Brit. M. J. 2:180 (July 26) 1952.

2. Douthwaite, A. H.: Medical Treatment of Peptic Ulcer, M. Press 227:195 (Feb. 27) 1952.

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References:

1. Jankelson, I.R.: Am. J. Digest. Dis. 14:11 (Jan.) 1947
2. Flexner, J. (Discussion): J.A.M.A. 129:899 (Apr. 7) 1945
3. Metcalf, R.G.: J. Maine M. A. 44:183 (July) 1953

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